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(71) Applicant (*for all designated States except US*): **MAXYGEN, INC.** [US/US]; 515 Galveston Drive, Redwood City, CA 94063 (US).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): **PAIDHUNGAT, Madan, M.** [IN/US]; 3525 Taraval St. #6, San Francisco, CA 94116 (US). **SAS, Ian** [CA/US]; 1017 Woodside Road, Redwood City, CA 94061 (US). **BOUQUIN, Thomas** [FR/DK]; Fasanvaenget 215, DK-2980 Kokkedal (DK). **LIN, David** [US/US]; 769 Bryn Mawr Court, Mountain View, CA 94043 (US). **CHEN, Teddy** [US/US]; 955 Escalon Ave., Apt 709, Sunnyvale, CA 94085 (US). **GUPTILL, Douglas** [US/US]; 1045 Burgoyne Street, Mountain View, CA 94043 (US). **BRIDEAU-ANDERSEN, Amy** [US/US]; 3 Sunup, Irivine, CA 92630 (US). **BASS, Steven, H.** [US/US]; 950 Parrott Drive, Hillsborough, CA 94010 (US). **PATTEN, Phillip, A.** [US/US]; 261 La Cuesta Drive, Portola Valley, CA 94028 (US).

(74) Agents: **KRUSE, Norman, J.** et al.; MAXYGEN, INC. - Patent Department, 515 Galveston Drive, Redwood City, CA 94063 (US).

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(54) Title: EVOLVED INTERFERON-ALPHA POLYPEPTIDES

(57) Abstract: The present invention provides evolved interferon-alpha polypeptides, and conjugates thereof, and nucleic acids encoding the polypeptides. The invention also includes compositions comprising these polypeptides, conjugates, and nucleic acids; cells containing or expressing the polypeptides, conjugates, and nucleic acids; methods of making the polypeptides, conjugates, and nucleic acids; and methods of using the polypeptides, conjugates, and nucleic acids.

EVOLVED INTERFERON-ALPHA POLYPEPTIDES

CROSS-REFERENCE TO RELATED APPLICATIONS

Pursuant to 35 U.S.C. §119(e), this application claims the benefit of U.S. Provisional Application Serial No. 60/682,769 filed on May 18, 2005, the disclosure of which is incorporated by reference herein in its entirety for all purposes.

FIELD OF THE INVENTION

The present invention relates generally to polynucleotides and polypeptides encoded therefrom, conjugates of the polypeptides, as well as vectors, cells, antibodies, and methods for using and producing the polynucleotides, polypeptides, and conjugates.

BACKGROUND OF THE INVENTION

Interferon-alphas are members of the diverse helical-bundle superfamily of cytokine genes (Sprang, S.R. et al. (1993) Curr. Opin. Struct. Biol. 3:815–827). The human interferon-alphas are encoded by a family of over 20 tandemly duplicated nonallelic genes and psuedogenes that share 85–98% sequence identity at the amino acid level (Henco, K. et al. (1985) J. Mol. Biol. 185:227–260). Genes which express active interferon-alpha proteins have been grouped into 13 families according to genetic loci. Known expressed human interferon-alpha proteins and their allelic variations are tabulated in Allen G. and Diaz M.O. (1996) J. Interferon and Cytokine Res. 16:181-184.

Interferon-alphas have been shown to inhibit various types of cellular proliferation, and are especially useful for the treatment of a variety of cellular proliferation disorders frequently associated with cancer, particularly hematologic malignancies such as leukemias. These proteins have shown antiproliferative activity against multiple myeloma, chronic lymphocytic leukemia, low-grade lymphoma, Kaposi's sarcoma, chronic myelogenous leukemia, renal-cell carcinoma, urinary bladder tumors and ovarian cancers (Bonnem, E.M. et al. (1984) J. Biol. Response Modifiers 3:580; Oldham, R.K. (1985) Hospital Practice 20:71).

Interferon-alphas are also useful against various types of viral infections (Finter, N.B. et al. (1991) Drugs 42(5):749). Interferon-alphas have activity against human papillomavirus infection, Hepatitis B, and Hepatitis C infections (Finter, N.B. et al., 1991, supra; Kashima, H. et al. (1988) Laryngoscope 98:334; Dusheiko, G.M. et al. (1986) J. Hematology 3 (Supple. 2):S199; Davis, GL et al. (1989) N. England J. Med. 321:1501). The role of interferons and interferon receptors in the pathogenesis of certain autoimmune and inflammatory diseases has also been investigated (Benoit, P. et al. (1993) J. Immunol. 150(3):707).

Although these proteins possess therapeutic value in the treatment of a number of diseases, they have not been optimized for use as pharmaceuticals. For example, dose-limiting toxicity, receptor cross-reactivity, and short serum half-lives significantly reduce the clinical utility of many of these cytokines (Dusheiko, G. (1997) Hepatology 26:112S–121S; Vial, T. and Descotes, J. (1994) Drug Experience 10:115–150; Funke, I. et al. (1994) Ann. Hematol. 68:49–52; Schomburg, A. et al. (1993) J. Cancer Res. Clin. Oncol. 119:745–755). Diverse and severe side effect profiles which accompany interferon administration include flu-like symptoms, fatigue, hallucination, fever, hepatic enzyme elevation, and leukopenia (Pontzer, C.H. et al. (1991) Cancer Res. 51:5304; Oldham, 1985, supra).

Hepatitis-C virus (HCV) is a nonhost integrated RNA virus with a very high rate of replication and is therefore associated with a large degree of genetic diversity. At least six genotypes and more than thirty subtypes of HCV RNA have been identified. HCV genotype has been shown to be a predictor of response to IFN-alpha therapy. Patients infected with HCV genotypes 2 and 3 have been found to generally respond well to interferon therapy. Patients infected with genotypes 4, 5 and 6 tend to respond less well. Patients infected with HCV genotype 1 tend to respond very poorly to interferon therapy, with about 50% of Genotype 1 patients classified as "nonresponders" towards IFN-alpha therapy. Genotype 1 is currently the most prevalent form of Hepatitis C, infecting approximately 70% of patients in the US and 50% of patients in Europe. Clearly, there is a pressing need for more effective therapies for HCV infection, particularly of the Genotype 1 variety.

There is genetic and biochemical evidence that Genotype 1 HCV (and other subtypes) actively attenuate the IFN-alpha signaling pathway by inhibiting key IFN

responsive proteins such as the dsRNA-activated serine/threonine protein kinase PKR (Katze M.G., *et al.* (2002) Nat. Rev. Immunol. 2(9):675-687) . As a likely consequence of this genetic diversity and active inhibition of the antiviral response, HCV (particularly Genotype 1) has the ability to escape the host's immune surveillance, leading to a high rate of chronic infection. The extensive genetic heterogeneity of HCV has important diagnostic and clinical implications, potentially accounting for variations in clinical course, difficulties in vaccine development, and lack of response to therapy.

The present invention addresses the need for interferon-alpha molecules which exhibit enhanced antiviral and/or immunomodulatory efficacy. The invention provides novel interferon-alpha polypeptides and polypeptide conjugates, nucleic acids encoding the polypeptides, and methods of using such molecules. Such molecules would be of beneficial use in a variety of applications, including, e.g., therapeutic and prophylactic treatments, particularly for viral infections and diseases and conditions associated with viral infections. The present invention fulfills these and other needs.

SUMMARY OF THE INVENTION

The present invention provides novel polypeptides, including variants thereof and fusion proteins comprising such polypeptides. The invention also provides conjugates comprising a polypeptide of the invention covalently linked to one or more non-polypeptide moieties. The invention also provides nucleic acids encoding any of the polypeptides of the invention, and vectors and host cells comprising such nucleic acids. In addition, the invention provides methods of making and using such polypeptides, conjugates, and nucleic acids, and other features apparent upon further review.

In one aspect, the invention provides an isolated or recombinant polypeptide, the polypeptide comprising a sequence identified as one of SEQ ID NO:1-SEQ ID NO:319. The invention also provides fusion proteins and conjugates comprising any of these polypeptides, nucleic acids encoding these polypeptides, and methods of making and using these polypeptides.

The invention also provides isolated or recombinant polypeptides which each comprise a sequence which differs in 0 to 16 amino acid positions from a sequence selected from SEQ ID NO:1 - SEQ ID NO:319, e.g., differs in 0, 2, 3, 4, 5, 6, 7, 8, 9, 10,

11, 12, 13, 14, 15, or 16 amino acid positions, e.g., in 0-16 amino acid positions, in 0-15 amino acid positions, in 0-14 amino acid positions, in 0-13 amino acid positions, in 0-12 amino acid positions, 0-11 amino acid positions, in 0-10 amino acid positions, in 0-9 amino acid positions, in 0-8 amino acid positions, in 0-7 amino acid positions, in 0-6 amino acid positions, in 0-5 amino acid positions, in 0-4 amino acid positions, in 0-3 amino acid positions, in 0-2 amino acid positions, or in 0-1 amino acid positions. Some such polypeptides comprise a sequence which differs in 0 to 16 amino acid positions from a sequence selected from SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:18, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:30, SEQ ID NO:46, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:94, SEQ ID NO:103, SEQ ID NO:107, SEQ ID NO:124, SEQ ID NO:127, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:148, SEQ ID NO:167, SEQ ID NO:171, SEQ ID NO:176, SEQ ID NO:179, SEQ ID NO:191, SEQ ID NO:195, SEQ ID NO:208, SEQ ID NO:232, SEQ ID NO:234, SEQ ID NO:258, SEQ ID NO:260, SEQ ID NO:262, SEQ ID NO:263, SEQ ID NO:266, SEQ ID NO:293, SEQ ID NO:296, SEQ ID NO:297, SEQ ID NO:298, SEQ ID NO:303, SEQ ID NO:306, SEQ ID NO:310, and SEQ ID NO:312. Some such polypeptides exhibit an interferon-alpha activity (such as, e.g., antiviral activity, T_H1 differentiation activity, and/or antiproliferative activity).

The invention also includes isolated or recombinant polypeptides which each comprise a sequence which differs in 0 to 16 amino acid positions from a sequence selected from SEQ ID NO:312 (M01); SEQ ID NO:262 (M04); SEQ ID NO:266 (M05); SEQ ID NO:232 (M23); SEQ ID NO:88 (M45); SEQ ID NO:297 (M20); SEQ ID NO:167 (M27); SEQ ID NO:107 (M09); SEQ ID NO:208 (M02); SEQ ID NO:94 (M33); SEQ ID NO:141 (M37); SEQ ID NO:46 (M30); SEQ ID NO:171 (M22); SEQ ID NO:310 (M24); SEQ ID NO:176 (M44); SEQ ID NO:26 (M31); SEQ ID NO:89 (M10); SEQ ID NO:296 (M14); SEQ ID NO:148 (M03); SEQ ID NO:18 (M46); SEQ ID NO:10 (M26); SEQ ID NO:87 (M21); SEQ ID NO:103 (M38); SEQ ID NO:234 (M28); SEQ ID NO:30 (M19); SEQ ID NO:179 (M11); SEQ ID NO:2 (M34); SEQ ID NO:260 (M07); SEQ ID NO:306 (M18); SEQ ID NO:140 (M40); SEQ ID NO:127 (M16); SEQ ID NO:293 (M25); SEQ ID NO:195 (M29); SEQ ID NO:191 (M36); SEQ ID NO:263 (M06); SEQ ID NO:1 (M32); SEQ ID NO:298 (M39); SEQ ID NO:24 (M42); SEQ ID NO:258 (M08); SEQ ID NO:124 (M35); SEQ ID NO:7 (M41); SEQ ID NO:9 (M12);

SEQ ID NO:303 (M17); and SEQ ID NO:6 (M43); e.g., differs in 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, or 16 amino acid positions, e.g., differs in 0-16 amino acid positions, 0-15 amino acid positions, in 0-14 amino acid positions, in 0-13 amino acid positions, in 0-12 amino acid positions, 0-11 amino acid positions, in 0-10 amino acid positions, in 0-9 amino acid positions, in 0-8 amino acid positions, in 0-7 amino acid positions, in 0-6 amino acid positions, in 0-5 amino acid positions, in 0-4 amino acid positions, in 0-3 amino acid positions, in 0-2 amino acid positions or in 0-1 amino acid positions, such as, for example, polypeptides described below. Some such polypeptides exhibit an interferon-alpha activity (such as, e.g., antiviral activity, T_H1 differentiation activity, and/or antiproliferative activity). Some such polypeptides exhibit at least two fold greater antiviral activity than human IFN-alpha 2a in a HeLa/EMCV antiviral assay. Some such polypeptides bind to the human interferon-alpha receptor with a higher affinity (lower EC_{50}) than that of IFN-alpha 2a. The polypeptides may further comprise one or more additional amino acid(s), such as, for example, a methionine added to the N-terminus. The invention also provides fusion proteins and conjugates comprising these polypeptides, and isolated or recombinant nucleic acids encoding these polypeptides.

The invention also provides conjugates comprising a polypeptide of the invention, such as any of the polypeptides of the invention described above, and at least one non-polypeptide moiety attached to an attachment group of the polypeptide, wherein the conjugate exhibits an interferon-alpha activity. In some instances, the non-polypeptide moiety is a polymer (for example, a polyalkylene oxide molecule, such as a polyethylene glycol (PEG), such as a monomethoxypolyethylene glycol (mPEG)), or a sugar moiety. The at least one non-polypeptide moiety may, for example, be attached to a cysteine, to a lysine, to the N-terminal amino group of the polypeptide, or to an *in vivo* glycosylation site of the polypeptide. The invention also provides methods of making and using such conjugates.

The invention also provides isolated or recombinant nucleic acids encoding any of the polypeptides of the invention. The invention also provides vectors and host cells comprising such nucleic acids, and methods of making polypeptides of the invention comprising culturing host cells comprising such nucleic acids.

In another aspect, the invention provides a method of inhibiting viral replication in virus-infected cells, the method comprising contacting the virus-infected cells with a

polypeptide or a conjugate of the invention. The invention also provides a method of reducing the number of copies of a virus in virus-infected cells, comprising contacting the virus-infected cells with a polypeptide or a conjugate of the invention.

In another aspect, the invention provides a method of treating a condition which is responsive to interferon-alpha, comprising administering to a subject afflicted with the condition a composition comprising a polypeptide of the invention or a conjugate of the invention in an amount effective to ameliorate a symptom associated with the condition. Such conditions include Chronic Hepatitis C Virus infection, Chronic Hepatitis B Virus infection, Hairy Cell Leukemia, Malignant Melanoma, Follicular Lymphoma, Condylomata Acuminata, AIDS-related Kaposi's Sarcoma, Non-Hodgkin's Lymphoma, Chronic Melogenous Leukemia, Basal Cell Carcinoma, Multiple Myeloma, carcinoid tumors, bladder cancer, Crohn's Disease, Cutaneous T Cell Lymphoma, Renal Cell Carcinoma, Multiple Sclerosis, and AIDS. The invention also includes the use of a composition comprising a polypeptide of the invention or a conjugate of the invention to treat a condition which is responsive to interferon-alpha, such as for example a condition described above.

These and other objects and features of the invention will become more fully apparent when the following detailed description is read in conjunction with the accompanying figures.

BRIEF DESCRIPTION OF THE FIGURES

Figure 1 shows an alignment of the sequence of a polypeptide of the invention (SEQ ID NO:1) with the following human interferon-alpha (huIFN-alpha) polypeptide sequences: huIFN-alpha 1a (SEQ ID NO:320), huIFN-alpha 2b (SEQ ID NO:321), huIFN-alpha 4b (SEQ ID NO:323), huIFN-alpha 5 (SEQ ID NO:324), huIFN-alpha 6 (SEQ ID NO:325), huIFN-alpha 7a (SEQ ID NO:326), huIFN-alpha 8b (SEQ ID NO:327), huIFN-alpha 10a (SEQ ID NO:328), huIFN-alpha 14a (SEQ ID NO:329), huIFN-alpha 16 (SEQ ID NO:330), huIFN-alpha 17b (SEQ ID NO:331) and huIFN-alpha 21b (SEQ ID NO:332). The naming conventions for the huIFN-alpha sequences are according to Allen G. and Diaz M.O. (1996) J. Interferon and Cytokine Res. 16:181-184. Amino acid residue positions in SEQ ID NOs:320-321 and 323-332 which are identical to

SEQ ID NO:1 are indicated with a period (.), and gaps in the sequence are indicated with a dash (-).

Figure 2 shows an alignment of the sequence of a polypeptide of the invention (SEQ ID NO:312) with human interferon-alpha polypeptide sequences SEQ ID NOs:320-321 and 323-332, as described above. Amino acid residue positions in SEQ ID NOs:320-321 and 323-332 which are identical to SEQ ID NO:312 are indicated with a period (.), and gaps in the sequence are indicated with a dash (-).

Figure 3 shows antiviral activity in a HeLa/EMCV assay, expressed as EC_{50} (ng/ml), for the following exemplary polypeptides of the invention: M04 (SEQ ID NO:262); M05 (SEQ ID NO:266); M23 (SEQ ID NO:232); M45 (SEQ ID NO:88); M01 (SEQ ID NO:312); M20 (SEQ ID NO:297); M27 (SEQ ID NO:167); M09 (SEQ ID NO:107); M02 (SEQ ID NO:208); M33 (SEQ ID NO:94); M37 (SEQ ID NO:141); M30 (SEQ ID NO:46); M22 (SEQ ID NO:171); M24 (SEQ ID NO:310); M44 (SEQ ID NO:176); M31 (SEQ ID NO:26); M10 (SEQ ID NO:89); M14 (SEQ ID NO:296); M03 (SEQ ID NO:148); M46 (SEQ ID NO:18); M26 (SEQ ID NO:10); M21 (SEQ ID NO:87); M38 (SEQ ID NO:103); M28 (SEQ ID NO:234); M19 (SEQ ID NO:30); M11 (SEQ ID NO:179); M34 (SEQ ID NO:2); M07 (SEQ ID NO:260); M18 (SEQ ID NO:306); M40 (SEQ ID NO:140); M16 (SEQ ID NO:127); M25 (SEQ ID NO:293); M29 (SEQ ID NO:195); M36 (SEQ ID NO:191); M06 (SEQ ID NO:263); M32 (SEQ ID NO:1); M39 (SEQ ID NO:298); M42 (SEQ ID NO:24); M08 (SEQ ID NO:258); M35 (SEQ ID NO:124); M41 (SEQ ID NO:7); M12 (SEQ ID NO:9); M17 (SEQ ID NO:303); and M43 (SEQ ID NO:6), as compared to the activity of reference interferon-alpha polypeptides huIFNα-2a (SEQ ID NO:322) and huIFNα-2b (SEQ ID NO:321).

Figure 4 shows the BLOSUM62 substitution matrix.

Figures 5A, 5B and 5C show examples of calculations of alignment scores used to determine optimal sequence alignments, using the following parameters: BLOSUM62 matrix, gap open penalty = 11, and gap extension penalty = 1. Figure 5A shows an alignment of residues 29-50 of SEQ ID NO:1 (upper) with residues 30-52 of SEQ ID NO:312 (lower). Figures 5B and 5C each show an alignment of residues 29-50 of SEQ ID NO:312 (upper) with residues 30-50 of SEQ ID NO:321 (lower), where Figure 5B shows the alignment score calculation without introduction of a gap in the alignment, and

Figure 5C shows the alignment score calculation with an introduction of a gap in the alignment.

Figures 6A-6V show the amino acid sequences of exemplary polypeptides of the invention, identified herein as SEQ ID NOs:1-319.

DETAILED DESCRIPTION OF THE INVENTION

DEFINITIONS

Unless otherwise defined herein or in the remainder of the specification, all technical and scientific terms used herein have the same meaning as commonly understood by those of ordinary skill in the art to which the invention belongs.

A "polypeptide sequence" (e.g., a protein, polypeptide, peptide, etc.) is a polymer of amino acids comprising naturally occurring amino acids or artificial amino acid analogues, or a character string representing an amino acid polymer, depending on context. Given the degeneracy of the genetic code, one or more nucleic acids, or the complementary nucleic acids thereof, that encode a specific polypeptide sequence can be determined from the polypeptide sequence.

A "polynucleotide sequence" (e.g., a nucleic acid, polynucleotide, oligonucleotide, etc.) is a polymer of nucleotides comprising nucleotides A,C,T,U,G, or other naturally occurring nucleotides or artificial nucleotide analogues, or a character string representing a nucleic acid, depending on context. Either the given nucleic acid or the complementary nucleic acid can be determined from any specified polynucleotide sequence.

Numbering of a given amino acid polymer or nucleic acid polymer "corresponds to" or is "relative to" the numbering of a selected amino acid polymer or nucleic acid polymer when the position of any given polymer component (e.g., amino acid, nucleotide, also referred to generically as a "residue") is designated by reference to the same or an equivalent position in the selected amino acid or nucleic acid polymer, rather than by the actual numerical position of the component in the given polymer. Thus, for example, the numbering of a given amino acid position in a given polypeptide sequence corresponds to the same or equivalent amino acid position in a selected polypeptide sequence used as a reference sequence.

An "equivalent position" (for example, an "equivalent amino acid position" or "equivalent nucleic acid position" or "equivalent residue position") is defined herein as a position (such as, an amino acid position or nucleic acid position or residue position) of a test polypeptide (or test polynucleotide) sequence which aligns with a corresponding position of a reference polypeptide (or reference polynucleotide) sequence, when optimally aligned using an alignment algorithm as described herein. The equivalent amino acid position of the test polypeptide need not have the same numerical position number as the corresponding position of the reference polypeptide; likewise, the equivalent nucleic acid position of the test polynucleotide need not have the same numerical position number as the corresponding position of the reference polynucleotide. As an example, Figure 1 shows the sequence of a polypeptide of the invention identified herein as SEQ ID NO:1 (clone M32) optimally aligned with various known human interferon-alpha polypeptide sequences. In this example, amino acid position number 90 of SEQ ID NO:1 (Tyr90, i.e. Y90) is considered to be an equivalent amino acid position to (i.e. is "equivalent to") that of amino acid position number 89 (Tyr89, i.e. Y89) of SEQ ID NO:321 (human IFN-alpha 2b), since amino acid number 90 of SEQ ID NO:1 aligns with amino acid number 89 of SEQ ID NO:321. In other words, amino acid position 90 of SEQ ID NO:1 "corresponds to" amino acid position 89 of SEQ ID NO:321. Likewise, residue Y90 (Tyr90) in SEQ ID NO:1 is understood to correspond to, for example, residue D90 (Asp90) in SEQ ID NO:312 (clone M01, see Figure 2), so that, for example, the substitution Y90F relative to SEQ ID NO:1 is understood to correspond to the substitution D90F relative to, e.g., SEQ ID NO:312, and so on.

Two polypeptide sequences are "optimally aligned" when they are aligned using defined parameters, i.e., a defined amino acid substitution matrix, gap existence penalty (also termed gap open penalty), and gap extension penalty, so as to arrive at the highest similarity score possible for that pair of sequences. The BLOSUM62 matrix (Henikoff and Henikoff (1992) Proc. Natl. Acad. Sci. USA 89(22):10915-10919) is often used as a default scoring substitution matrix in polypeptide sequence alignment algorithms (such as BLASTP). The gap existence penalty is imposed for the introduction of a single amino acid gap in one of the aligned sequences, and the gap extension penalty is imposed for each residue position in the gap. Unless otherwise stated, alignment parameters employed herein are: BLOSUM62 scoring matrix, gap existence penalty = 11, and gap

extension penalty = 1. The alignment score is defined by the amino acid positions of each sequence at which the alignment begins and ends (e.g. the alignment window), and optionally by the insertion of a gap or multiple gaps into one or both sequences, so as to arrive at the highest possible similarity score, as described in more detail below in the section entitled *"Percent Sequence Identity"*.

The terminology used for identifying amino acid positions and amino acid substitutions is illustrated as follows: Q52 indicates position number 52 is occupied by a glutamine (Gln) residue in a reference amino acid sequence, such as SEQ ID NO:1. Q52E indicates that the glutamine residue of position 52 has been substituted with a glutamic acid (Glu) residue. Alternative substitutions are indicated with a "/", e.g., Q52E/P means an amino acid sequence in which the glutamine residue at position 52 is substituted with a glutamic acid residue or a proline residue. Multiple substitutions may sometimes be indicated with a "+", e.g. A51T + Q52E/P indicates an amino acid sequence which contains a substitution of the alanine residue at position 51 with an threonine residue and a subsitution of the glutamine residue at position 52 with a glutamic acid residue or a proline residue. Deletions are indicated by an asterix. For example, Q52* indicates that the glutamine residue at position 52 has been deleted. Deletions of two or more continuous amino acids may be indicated as follows, e.g., R161*-E166* indicates the deletion of residues R161-E166 inclusive (that is, residues 161, 162, 163, 164, 164, and 166 are deleted). Insertions are indicated the following way: Insertion of an additional serine residue after the glutamine residue located at position 52 is indicated as Q52QS. Combined substitutions and insertions are indicated in the following way: Substitution of the glutamine residue at position 52 with a serine residue and insertion of an alanine residue after the position 52 amino acid residue is indicated as Q52SA.

Unless otherwise indicated, the position numbering of amino acid residues recited herein is relative to the amino acid sequence SEQ ID NO:1. It is to be understood that while the examples and modifications to the parent polypeptide may be provided herein relative to the sequence SEQ ID NO:1 (or relative to another specified sequence), the examples pertain to other polypeptides of the invention, and the modifications described herein may be made in equivalent amino acid positions (as described above) of any of the other polypeptides described herein. Thus, as an example, the substitution Y90F relative

to SEQ ID NO:1 is understood to correspond to the substitution D90F in SEQ ID NO:312, and so on.

The term "exhibiting (e.g., exhibits, or having, or has) an interferon-alpha activity" is intended to indicate that the polypeptide or conjugate of the invention has at least one activity exhibited by a reference interferon-alpha polypeptide (such as, for example, a human interferon-alpha polypeptide, e.g., huIFN-alpha 2b identified herein as SEQ ID NO:321, huIFN-alpha 2a identified herein as SEQ ID NO:322, hIFN-alpha 8b identified herein as SEQ ID NO:327, or any other interferon alpha polypeptide known in the art, such as, for example, those listed in Allen G. and Diaz M.O. (1996, *supra*)). Such activity includes the ability to signal through an interferon-alpha receptor, as evidenced by, for example, one or more of: inhibition of viral replication or inhibition of cytopathic effect in virus-infected cells ("antiviral activity"); enhancement of differentiation of naïve T-cells to a T_H1 phenotype and/or suppression of differentiation of naïve T-cells to a T_H2 phenotype ("T_H1 differentiation activity"); or inhibition of cell proliferation ("antiproliferative activity"). The one or more interferon-alpha activity is assayed using assays known in the art and/or described in the Examples.

A polypeptide or a conjugate exhibiting an interferon-alpha activity is considered to have such activity when it displays a measurable activity, e.g., a measurable antiviral activity, antiproliferative activity, or T_H1 differentiation activity (e.g., as determined by assays known in the art and/or described in the Examples). One of skill in the art recognizes that what constitutes a measurable activity depends in part on the nature of the assay being undertaken, but as a general guideline a measurable activity is one in which the assay signal generated in the presence of the test compound (e.g., a polypeptide of the invention) is quantifiably different than the assay signal generated in the absence of the test compound. It is to be understood that a polypeptide or conjugate of the invention need not exhibit all of the known activities of a particular reference interferon-alpha, or exhibit such activities to the same extent as the reference interferon-alpha. In some instances the activity exhibited by a polypeptide or conjugate of the invention (as evidenced, e.g., by an EC_{50}, specific activity, or other value related to activity) may be about equal to, be less than, or be greater than that of the particular activity exhibited by the reference interferon-alpha.

A "variant" is a polypeptide comprising a sequence which differs in one or more amino acid position(s) from that of a parent polypeptide sequence. For example, a variant may comprise a sequence which differs from the parent polypeptides sequence in up to 10% of the total number of residues of the parent polypeptide sequence, such as in up to 8% of the residues, e.g., in up to 6%, 5%, 4%, 3% 2% or 1% of the total number of residue of the parent polypeptide sequence. For example, a variant of SEQ ID NO:1 may comprise a sequence which differs from SEQ ID NO:1 in 1-16 amino acid positions (such as in 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, or 16 amino acid positions), e.g. in 1-15 amino acid positions, in 1-14 amino acid positions, in 1-13 amino acid positions, in 1-12 amino acid positions, in 1-11 amino acid positions, in 1-10 amino acid positions, in 1-9 amino acid positions, in 1-8 amino acid positions, in 1-7 amino acid positions, in 1-6 amino acid positions, in 1-5 amino acid positions, in 1-4 amino acid positions, in 1-3 amino acid positions, or in 1-2 amino acid positions.

The term "parent polypeptide" or "parent interferon-alpha" is intended to indicate the polypeptide sequence to be modified in accordance with the present invention. The parent polypeptide sequence may be that of a naturally occurring IFN-alpha (such as a mammalian IFN-alpha, e.g., a primate IFN-alpha, such as a human IFN-alpha, such as a huIFN-alpha polypeptide identified herein as SEQ ID NOs:320-332, or other huIFN-alpha sequence such as those described herein and/or in Allen G. and Diaz M.O. (1996), *supra*). The parent polypeptide sequence may be that of a non-naturally occurring (i.e., "synthetic") interferon-alpha, such as IFN-alpha Con1 (SEQ ID NO:333). In some instances, the parent polypeptide to be modified may itself be a polypeptide of the invention, such as, for example, any one of SEQ ID NOs:1-319.

"Naturally occurring" as applied to an object refers to the fact that the object can be found in nature as distinct from being artificially produced by man. For example, a polypeptide or polynucleotide sequence that is present in an organism (including viruses, bacteria, protozoa, insects, plants or mammalian tissue) that can be isolated from a source in nature and which has not been intentionally modified by man in the laboratory is naturally occurring. "Non-naturally occurring" (also termed "synthetic" or "artificial") as applied to an object means that the object is not naturally-occurring -- i.e., the object cannot be found in nature as distinct from being artificially produced by man.

A "fragment" or "subsequence" is any portion of an entire sequence, up to but not including the entire sequence. Thus, a fragment or subsequence refers to a sequence of amino acids or nucleic acids that comprises a part of a longer sequence of amino acids (e.g., polypeptide) or nucleic acids (e.g., polynucleotide).

One type of fragment contemplated by the present invention is a fragment in which amino acid residues are removed from the N-terminus or the C-terminus of the parent polypeptide (or both); such a polypeptide is considered to be "N-terminally truncated" or "C-terminally truncated", respectively. Deletion of at least the first four amino acids from the N-terminus does not significantly affect interferon-alpha activity (Lydon, N.B. *et al.* (1985) Biochemistry 24: 4131-41). Furthermore, variants retaining interferon-alpha activity have been described wherein between 7 and 11 amino acids have been deleted from the C-terminus (Cheetham B.F. *et al.* (1991) Antiviral Res. 15(1):27-39; Chang N.T. *et al.* (1983) Arch. Biochem Biophys. 221(2): 585-589; Franke A.E. *et al.* (1982) DNA 1(3):223-230).

A "receptor" e.g., an "interferon-alpha receptor" (also known as a "Type I interferon receptor") is a receptor which is activated in cells by an interferon-alpha, e.g., binds an interferon-alpha and initiates intracellular signaling, such as a type I interferon receptor comprising receptor subunits IFNAR-2 and IFNAR-1 (Domanski et al. (1998) J. Biol. Chem. 273(6):3144-3147; Mogensen et al., (1999) Journal of Interferon and Cytokine Research, 19:1069-1098). In the context of this invention, receptor is also meant to include truncated forms of a full-length receptor molecule, such as for example a receptor molecule which lacks a membrane-binding portion, such as a soluble form of a receptor molecule (also known as a "soluble receptor") which comprises an extracelluar binding domain, which binds an interferon-alpha, but may not necessarily bind to a membrane and/or initiate intracellular signaling.

A "specific binding affinity" between two molecules, e.g., a ligand and a receptor, means a preferential binding of one molecule for another in a mixture of molecules. The binding of the molecules is typically considered specific if the binding affinity is about 1 x 10^4 M^{-1} to about 1 x 10^9 M^{-1} or greater (i.e., K_D of about 10^{-4} M to 10^{-9} M or less). Binding affinity of a ligand and a receptor may be measured by standard techniques known to those of skill in the art. Non-limiting examples of well-known techniques for measuring binding affinities include Biacore® technology (Biacore AB, Sweden),

isothermal titration microcalorimetry (MicroCal LLC, Northampton, MA USA), ELISA, and flow cytometry (e.g., FACS). For example, flow cytometric methods may be used to select for populations of molecules (such as, for example, cell surface-displayed ligands) which specifically bind to the associated binding pair member (such as a receptor). Ligand-receptor complexes may be detected and sorted by fluorescence (for example, by reacting the complex with a fluorescent antibody that recognizes the complex, or by reacting a complex comprising a biotinylated ligand with a streptavidin-conjugated fluroescent probe). Molecules of interest which bind an associated binding pair member (e.g., receptor) are pooled and re-sorted in the presence of lower concentrations of receptor. By performing multiple rounds of cell sorting in the presence of decreasing concentrations of receptor (an exemplary concentration range being on the order of 10^{-6} M down to 10^{-9} M, i.e., 1 micromolar (μM) down to 1 nanomolar (nM), or less, depending on the nature of the ligand-receptor interaction), enriched populations of molecules exhibiting specific binding affinity for the receptor may be obtained.

A polypeptide, nucleic acid, or other component is "isolated" when it is partially or completely separated from components with which it is normally associated (other peptides, polypeptides, proteins (including complexes, e.g., polymerases and ribosomes which may accompany a native sequence), nucleic acids, cells, synthetic reagents, cellular contaminants, cellular components, etc.), e.g., such as from other components with which it is normally associated in the cell from which it was originally derived. A polypeptide, nucleic acid, or other component is isolated when it is partially or completely recovered or separated from other components of its natural environment such that it is the predominant species present in a composition, mixture, or collection of components (i.e., on a molar basis it is more abundant than any other individual species in the composition). In some instances, the preparation consists of more than about 60%, 70% or 75%, typically more than about 80%, or preferably more than about 90% of the isolated species.

A "substantially pure" or "isolated" nucleic acid (e.g., RNA or DNA), polypeptide, protein, or composition also means where the object species (e.g., nucleic acid or polypeptide) comprises at least about 50, 60, or 70 percent by weight (on a molar basis) of all macromolecular species present. A substantially pure or isolated composition can also comprise at least about 80, 90, or 95 percent by weight of all macromolecular species

present in the composition. An isolated object species can also be purified to essential homogeneity (contaminant species cannot be detected in the composition by conventional detection methods) wherein the composition consists essentially of derivatives of a single macromolecular species. The term "purified" generally denotes that a nucleic acid, polypeptide, or protein gives rise to essentially one band in an electrophoretic gel. It typically means that the nucleic acid, polypeptide, or protein is at least about 50% pure, 60% pure, 70% pure, 75% pure, more preferably at least about 85% pure, and most preferably at least about 99% pure.

The term "isolated nucleic acid" may refer to a nucleic acid (e.g., DNA or RNA) that is not immediately contiguous with both of the coding sequences with which it is immediately contiguous (i.e., one at the 5' and one at the 3' end) in the naturally occurring genome of the organism from which the nucleic acid of the invention is derived. Thus, this term includes, e.g., a cDNA or a genomic DNA fragment produced by polymerase chain reaction (PCR) or restriction endonuclease treatment, whether such cDNA or genomic DNA fragment is incorporated into a vector, integrated into the genome of the same or a different species than the organism, including, e.g., a virus, from which it was originally derived, linked to an additional coding sequence to form a hybrid gene encoding a chimeric polypeptide, or independent of any other DNA sequences. The DNA may be double-stranded or single-stranded, sense or antisense.

A "recombinant polynucleotide" or a "recombinant polypeptide" is a non-naturally occurring polynucleotide or polypeptide which may include nucleic acid or amino acid sequences, respectively, from more than one source nucleic acid or polypeptide, which source nucleic acid or polypeptide can be a naturally occurring nucleic acid or polypeptide, or can itself have been subjected to mutagenesis or other type of modification. A nucleic acid or polypeptide may be deemed "recombinant" when it is synthetic or artificial or engineered, or derived from a synthetic or artificial or engineered polypeptide or nucleic acid. A recombinant nucleic acid (e.g., DNA or RNA) can be made by the combination (e.g., artificial combination) of at least two segments of sequence that are not typically included together, not typically associated with one another, or are otherwise typically separated from one another. A recombinant nucleic acid can comprise a nucleic acid molecule formed by the joining together or combination of nucleic acid segments from different sources and/or artificially synthesized. A

"recombinant polypeptide" often refers to a polypeptide that results from a cloned or recombinant nucleic acid. The source polynucleotides or polypeptides from which the different nucleic acid or amino acid sequences are derived are sometimes homologous (i.e., have, or encode a polypeptide that encodes, the same or a similar structure and/or function), and are often from different isolates, serotypes, strains, species, of organism or from different disease states, for example.

The term "recombinant" when used with reference, e.g., to a cell, polynucleotide, vector, protein, or polypeptide typically indicates that the cell, polynucleotide, or vector has been modified by the introduction of a heterologous (or foreign) nucleic acid or the alteration of a native nucleic acid, or that the protein or polypeptide has been modified by the introduction of a heterologous amino acid, or that the cell is derived from a cell so modified. Recombinant cells express nucleic acid sequences that are not found in the native (non-recombinant) form of the cell or express native nucleic acid sequences that would otherwise be abnormally expressed, under-expressed, or not expressed at all. The term "recombinant" when used with reference to a cell indicates that the cell replicates a heterologous nucleic acid, or expresses a polypeptide encoded by a heterologous nucleic acid. Recombinant cells can contain coding sequences that are not found within the native (non-recombinant) form of the cell. Recombinant cells can also contain coding sequences found in the native form of the cell wherein the coding sequences are modified and re-introduced into the cell by artificial means. The term also encompasses cells that contain a nucleic acid endogenous to the cell that has been modified without removing the nucleic acid from the cell; such modifications include those obtained by gene replacement, site-specific mutation, recombination, and related techniques.

The term "recombinantly produced" refers to an artificial combination usually accomplished by either chemical synthesis means, recursive sequence recombination of nucleic acid segments or other diversity generation methods (such as, e.g., shuffling) of nucleotides, or manipulation of isolated segments of nucleic acids, e.g., by genetic engineering techniques known to those of ordinary skill in the art. "Recombinantly expressed" typically refers to techniques for the production of a recombinant nucleic acid *in vitro* and transfer of the recombinant nucleic acid into cells *in vivo, in vitro, or ex vivo* where it may be expressed or propagated.

A "recombinant expression cassette" or simply an "expression cassette" is a nucleic acid construct, generated recombinantly or synthetically, with nucleic acid elements that are capable of effecting expression of a structural gene in hosts compatible with such sequences. Expression cassettes include at least promoters and optionally, transcription termination signals. Typically, the recombinant expression cassette includes a nucleic acid to be transcribed (e.g., a nucleic acid encoding a desired polypeptide), and a promoter. Additional factors necessary or helpful in effecting expression may also be used as described herein. For example, an expression cassette can also include nucleotide sequences that encode a signal sequence that directs secretion of an expressed protein from the host cell. Transcription termination signals, enhancers, and other nucleic acid sequences that influence gene expression, can also be included in an expression cassette.

An "immunogen" refers to a substance capable of provoking an immune response, and includes, e.g., antigens, autoantigens that play a role in induction of autoimmune diseases, and tumor-associated antigens expressed on cancer cells. An immune response generally refers to the development of a cellular or antibody-mediated response to an agent, such as an antigen or fragment thereof or nucleic acid encoding such agent. In some instances, such a response comprises a production of at least one or a combination of CTLs, B cells, or various classes of T cells that are directed specifically to antigen-presenting cells expressing the antigen of interest.

An "antigen" refers to a substance that is capable of eliciting the formation of antibodies in a host or generating a specific population of lymphocytes reactive with that substance. Antigens are typically macromolecules (e.g., proteins and polysaccharides) that are foreign to the host.

An "adjuvant" refers to a substance that enhances an antigen's immune-stimulating properties or the pharmacological effect(s) of a drug. An adjuvant may non-specifically enhance the immune response to an antigen. "Freund's Complete Adjuvant," for example, is an emulsion of oil and water containing an immunogen, an emulsifying agent and mycobacteria. Another example, "Freund's incomplete adjuvant," is the same, but without mycobacteria.

A vector is a component or composition for facilitating cell transduction or transfection by a selected nucleic acid, or expression of the nucleic acid in the cell. Vectors include, e.g., plasmids, cosmids, viruses, YACs, bacteria, poly-lysine, etc. An

"expression vector" is a nucleic acid construct or sequence, generated recombinantly or synthetically, with a series of specific nucleic acid elements that permit transcription of a particular nucleic acid in a host cell. The expression vector can be part of a plasmid, virus, or nucleic acid fragment. The expression vector typically includes a nucleic acid to be transcribed operably linked to a promoter. The nucleic acid to be transcribed is typically under the direction or control of the promoter.

"Substantially the entire length of a polynucleotide sequence" or "substantially the entire length of a polypeptide sequence" refers to at least 50%, generally at least about 60%, 70%, or 75%, usually at least about 80%, or typically at least about 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more of a length of a polynucleotide sequence or polypeptide sequence.

The term "immunoassay" includes an assay that uses an antibody or immunogen to bind or specifically bind an antigen. The immunoassay is typically characterized by the use of specific binding properties of a particular antibody to isolate, target, and/or quantify the antigen.

The term "subject" as used herein includes, but is not limited to, an organism; a mammal, including, e.g., a human, non-human primate (e.g., baboon, orangutan, monkey), mouse, pig, cow, goat, cat, rabbit, rat, guinea pig, hamster, horse, monkey, sheep, or other non-human mammal; a non-mammal, including, e.g., a non-mammalian vertebrate, such as a bird (e.g., a chicken or duck) or a fish, and a non-mammalian invertebrate.

The term "pharmaceutical composition" means a composition suitable for pharmaceutical use in a subject, including an animal or human. A pharmaceutical composition generally comprises an effective amount of an active agent and a carrier, including, e.g., a pharmaceutically acceptable carrier.

The term "effective amount" means a dosage or amount sufficient to produce a desired result. The desired result may comprise an objective or subjective improvement in the recipient of the dosage or amount.

A "prophylactic treatment" is a treatment administered to a subject who does not display signs or symptoms of a disease, pathology, or medical disorder, or displays only early signs or symptoms of a disease, pathology, or disorder, such that treatment is administered for the purpose of diminishing, preventing, or decreasing the risk of

developing the disease, pathology, or medical disorder. A prophylactic treatment functions as a preventative treatment against a disease or disorder. A "prophylactic activity" is an activity of an agent, such as a nucleic acid, vector, gene, polypeptide, protein, substance, or composition thereof that, when administered to a subject who does not display signs or symptoms of pathology, disease or disorder, or who displays only early signs or symptoms of pathology, disease, or disorder, diminishes, prevents, or decreases the risk of the subject developing a pathology, disease, or disorder. A "prophylactically useful" agent or compound (e.g., nucleic acid or polypeptide) refers to an agent or compound that is useful in diminishing, preventing, treating, or decreasing development of pathology, disease or disorder.

A "therapeutic treatment" is a treatment administered to a subject who displays symptoms or signs of pathology, disease, or disorder, in which treatment is administered to the subject for the purpose of diminishing or eliminating those signs or symptoms of pathology, disease, or disorder. A "therapeutic activity" is an activity of an agent, such as a nucleic acid, vector, gene, polypeptide, protein, substance, or composition thereof, that eliminates or diminishes signs or symptoms of pathology, disease or disorder, when administered to a subject suffering from such signs or symptoms. A "therapeutically useful" agent or compound (e.g., nucleic acid or polypeptide) indicates that an agent or compound is useful in diminishing, treating, or eliminating such signs or symptoms of a pathology, disease or disorder.

The term "gene" broadly refers to any segment of DNA associated with a biological function. Genes include coding sequences and/or regulatory sequences required for their expression. Genes also include non-expressed DNA nucleic acid segments that, e.g., form recognition sequences for other proteins (e.g., promoter, enhancer, or other regulatory regions). Genes can be obtained from a variety of sources, including cloning from a source of interest or synthesizing from known or predicted sequence information, and may include sequences designed to have desired parameters.

Generally, the nomenclature used hereafter and the laboratory procedures in cell culture, molecular genetics, molecular biology, nucleic acid chemistry, and protein chemistry described below are those well known and commonly employed by those of ordinary skill in the art. Standard techniques, such as described in Sambrook et al., Molecular Cloning - A Laboratory Manual (2nd Ed.), Vols. 1-3, Cold Spring Harbor

Laboratory, Cold Spring Harbor, New York, 1989 (hereinafter "Sambrook") and Current Protocols in Molecular Biology, F. M. Ausubel et al., eds., Current Protocols, a joint venture between Greene Publishing Associates, Inc. and John Wiley & Sons, Inc. (1994, supplemented through 1999) (hereinafter "Ausubel"), are used for recombinant nucleic acid methods, nucleic acid synthesis, cell culture methods, and transgene incorporation, e.g., electroporation, injection, gene gun, impressing through the skin, and lipofection. Generally, oligonucleotide synthesis and purification steps are performed according to specifications. The techniques and procedures are generally performed according to conventional methods in the art and various general references which are provided throughout this document. The procedures therein are believed to be well known to those of ordinary skill in the art and are provided for the convenience of the reader.

As used herein, an "antibody" refers to a protein comprising one or more polypeptides substantially or partially encoded by immunoglobulin genes or fragments of immunoglobulin genes. The term antibody is used to mean whole antibodies and binding fragments thereof. The recognized immunoglobulin genes include the kappa, lambda, alpha, gamma, delta, epsilon and mu constant region genes, as well as myriad immunoglobulin variable region genes. Light chains are classified as either kappa or lambda. Heavy chains are classified as gamma, mu, alpha, delta, or epsilon, which in turn define the immunoglobulin classes, IgG, IgM, IgA, IgD and IgE, respectively. A typical immunoglobulin (e.g., antibody) structural unit comprises a tetramer. Each tetramer is composed of two identical pairs of polypeptide chains, each pair having one "light" (about 25 KDa) and one "heavy" chain (about 50-70 KDa). The N-terminus of each chain defines a variable region of about 100 to 110 or more amino acids primarily responsible for antigen recognition. The terms variable light chain (V_L) and variable heavy chain (V_H) refer to these light and heavy chains, respectively.

Antibodies also include single-armed composite monoclonal antibodies, single chain antibodies, including single chain Fv (sFv) antibodies in which a variable heavy and a variable light chain are joined together (directly or through a peptide linker) to form a continuous polypeptide, as well as diabodies, tribodies, and tetrabodies (Pack et al. (1995) J Mol Biol 246:28; Biotechnol 11:1271; and Biochemistry 31:1579). The antibodies are, *e.g.*, polyclonal, monoclonal, chimeric, humanized, single chain, Fab fragments, fragments produced by an Fab expression library, or the like.

The term "epitope" means a protein determinant capable of specific binding to an antibody. Epitopes usually consist of chemically active surface groupings of molecules such as amino acids or sugar side chains and usually have specific three dimensional structural characteristics, as well as specific charge characteristics. Conformational and nonconformational epitopes are distinguished in that the binding to the former but not the latter is lost in the presence of denaturing solvents.

An "antigen-binding fragment" of an antibody is a peptide or polypeptide fragment of the antibody that binds an antigen. An antigen-binding site is formed by those amino acids of the antibody that contribute to, are involved in, or affect the binding of the antigen. See Scott, T.A. and Mercer, E.I., Concise Encyclopedia: Biochemistry and Molecular Biology (de Gruyter, 3d ed. 1997), and Watson, J.D. et al., Recombinant DNA (2d ed. 1992) (hereinafter "Watson, Recombinant DNA"), each of which is incorporated herein by reference in its entirety for all purposes.

The term "screening" describes, in general, a process that identifies optimal molecules of the present invention, such as, e.g., polypeptides of the invention, and nucleic acids encoding such molecules. Several properties of these respective molecules can be used in screening, for example: ability of a molecule to bind a ligand or to a receptor, to inhibit cell proliferation, to inhibit viral replication in virus-infected cells, to induce or inhibit cellular cytokine production, to alter an immune response (e.g., induce or inhibit a desired immune response), in a test system or an *in vitro, ex vivo* or *in vivo* application. In the case of antigens, several properties of the antigen can be used in selection and screening including antigen expression, folding, stability, immunogenicity and presence of epitopes from several related antigens.

"Selection" is a form of screening in which identification and physical separation are achieved simultaneously. One mode of selection is genetic selection, which may be accomplished, for example, by expression of a selection marker, which in some circumstances allows cells expressing the marker to survive while other cells die (or vice versa). Selection markers include drug and toxin resistance genes, and the like. Screening markers include, for example, luciferase, beta-galactosidase and green fluorescent protein, and the like. Another mode of selection involves physical sorting based on a detectable event, such as binding of a ligand to a receptor, reaction of a substrate with an enzyme, or any other physical process which can generate a detectable signal either

directly (e.g., by utilizing a chromogenic/fluorogenic substrate or ligand) or indirectly (e.g., by reacting with a chromogenic/fluorogenic secondary antibody or chomogenic/fluorogenic ligand).

Selection by physical sorting may by accomplished by a variety of methods, such as by flow cytometry, e.g. in whole cell or microdroplet formats. For example, libraries may be subcloned into a surface display vector to permit expression of polypeptides on the cell surface. Libraries of surface-expressed polypeptides may then be pre-enriched for those polypeptides which bind to a receptor, using flow cytometry. For instance, cells displaying polypeptides which bind the receptor may be detected using a fluorescent-labeled anti-receptor antibody, which, when bound to the receptor, indirectly labels the cells owing to the interaction of the receptor with the surface-displayed polypeptide. Cells which are fluorescently labeled in this manner may then be sorted by flow cytometry, which pre-enriches the library for members which encode expressed and folded polypeptides that bind the receptor. Libraries pre-enriched for receptor binders may then be subjected to a selection using a competition assay to further enrich for members encoding polypeptides that bind tightly to the receptor and/or exhibit a slow off-rate from the receptor, relative to a reference polypeptide. In this approach, receptor is added to a population of cells expressing polypeptides on the cell surface. The cells are washed, and then a reference polypeptide is added. Cell populations are sorted by flow cytometry after various times to select for surface-displayed polypeptides which remained bound to the receptor for increasing periods of time in the presence of the reference polypeptide. Cell populations selected in this manner are expected to be enriched for library members which encode polypeptides exhibiting tighter binding to the cognate receptor, and permits the isolation and identification of polypeptides with activities associated with tight receptor binding.

An “exogenous” nucleic acid,” “exogenous DNA segment,” “heterologous sequence,” or “heterologous nucleic acid,” as used herein, is one that originates from a source foreign to the particular host cell, or, if from the same source, is modified from its original form. Thus, a heterologous gene in a host cell includes a gene that is endogenous to the particular host cell, but has been modified. Modification of a heterologous sequence in the applications described herein typically occurs through the use of recursive sequence recombination. The terms refer to a DNA segment which is foreign or

heterologous to the cell, or homologous to the cell but in a position within the host cell nucleic acid in which the element is not ordinarily found. Exogenous DNA segments are expressed to yield exogenous polypeptides.

The term "nucleic acid" refers to deoxyribonucleotides or ribonucleotides and polymers thereof in either single- or double-stranded form. Unless specifically limited, the term encompasses nucleic acids containing known analogues of natural nucleotides which have similar binding properties as the reference nucleic acid and are metabolized in a manner similar to naturally occurring nucleotides. Unless otherwise indicated, a particular nucleic acid sequence also implicitly encompasses conservatively modified variants thereof (e.g., degenerate codon substitutions) and complementary sequences and as well as the sequence explicitly indicated. Specifically, degenerate codon substitutions may be achieved by generating sequences in which the third position of one or more selected (or all) codons is substituted with mixed-base and/or deoxyinosine residues (Batzer et al. (1991) Nucleic Acid Res 19:5081; Ohtsuka et al. (1985) J Biol Chem 260:2605-2608; Cassol et al. (1992) ; Rossolini et al. (1994) Mol Cell Probes 8:91-98). The term nucleic acid is used interchangeably with gene, cDNA, and mRNA encoded by a gene.

"Nucleic acid derived from a gene" refers to a nucleic acid for whose synthesis the gene, or a subsequence thereof, has ultimately served as a template. Thus, an mRNA, a cDNA reverse transcribed from an mRNA, an RNA transcribed from that cDNA, a DNA amplified from the cDNA, an RNA transcribed from the amplified DNA, *etc.*, are all derived from the gene and detection of such derived products is indicative of the presence and/or abundance of the original gene and/or gene transcript in a sample.

A nucleic acid is "operably linked" when it is placed into a functional relationship with another nucleic acid sequence. For instance, a promoter or enhancer is operably linked to a coding sequence if it increases the transcription of the coding sequence. Operably linked means that the DNA sequences being linked are typically contiguous and, where necessary to join two protein coding regions, contiguous and in reading frame. However, since enhancers generally function when separated from the promoter by several kilobases and intronic sequences may be of variable lengths, some polynucleotide elements may be operably linked but not contiguous.

The term "cytokine" includes, for example, interleukins, interferons, chemokines, hematopoietic growth factors, tumor necrosis factors and transforming growth factors. In general these are low molecular weight proteins that regulate maturation, activation, proliferation, and differentiation of cells of the immune system.

In the present description and claims, any reference to "a" component, e.g. in the context of a non-polypeptide moiety, an amino acid residue, a substitution, a buffer, a cation, etc., is intended to refer to one or more of such components, unless stated otherwise or unless it is clear from the particular context that this is not the case. For example, the expression "a component selected from the group consisting of A, B and C" is intended to include all combinations of A, B and C, *e.g.*, A, B, C, A+B, A+C, B+C or A+B+C.

Various additional terms are defined or otherwise characterized herein.

MOLECULES AND METHODS OF THE INVENTION

Molecules of the invention (e.g., polypeptides of the invention, conjugates of the invention, and nucleic acids encoding said polypeptides) are useful for the treatment of diseases and disorders which are responsive to treatment by interferon-alpha, particularly diseases associated with viral infection, such as, for example, infection by HCV.

Patients with chronic HCV infection have viral loads typically in the range of 10^4 – 10^7 copies of HCV RNA/ml of serum prior to treatment. Upon treatment with IFN-alpha, viral load in these patients characteristically undergoes two distinct log-linear phases of decline (Neumann A.U., *et al.* (1998) Science 282:103-107). The initial rapid drop in viral load that occurs within the first two days of IFN-alpha therapy is believed to be due to interferon-alpha mediated reduction in virus production in the infected liver cells and concomitant protection of naïve cells against infection. The rate of viral production reaches a new steady state at about two days, at which time a second less rapid log-linear phase of viral clearance is observed. This second phase of viral clearance is generally believed to be due in part to T-cell mediated killing of infected liver cells (Neumann, *et al., supra*). IFN-alpha is believed to play a key role in this biological response through the stimulation of antigen specific T cells to differentiate into T_H1 cells. Furthermore, the mode of action of Ribavirin is believed to be due to augmentation of the T_H1 response, and is thought to be the mechanistic basis of its efficacy in combination therapy with IFN-alpha. HCV-infected patients who are non-responsive to interferon-alpha therapies

currently in use (generally termed "non-responders") exhibit much shallower viral load clearance profiles.

Although the present invention is not intended to be limited by a particular theory of underlying mechanism, it is proposed that antiviral activity in surrogate assay systems (such as those described in more detail herein) may be predictive of interferon-alpha efficacy, in for example the first phase of viral clearance. Exemplary antiviral assays, described in the Examples section, monitor the effectiveness of IFN-alpha in protecting against the cytopathic effect of Encephalomyocarditis Virus (EMCV) HeLa human cervical carcinoma cells as a surrogate system for effectiveness against HCV in human liver cells. Other useful virus / cell assay systems include EMCV in WISH human amnion-derived cells, EMCV in in HuH7 human liver-derived cells, Vesicular Stomatitis Virus (VSV) in HuH7 cells, Vaccinia Virus (VV) in HeLa cells, Yellow Fever Virus (YFV) in HepG2 human hepatocarcinoma cells, as well as Human Immunodeficiency Virus (HIV) in primary CD4+ T-cells. Example 2 and Figure 3 shows antiviral activities of representative polypeptides of the invention in the EMCV/HeLa antiviral assay.

Other surrogate assay systems useful for monitoring effectiveness against HCV in infected hepatocytes include HCV replicon systems, as described, for example, by Lohmann V., *et al.*, (1999) Science 285(5424):285-293; Randall G. and Rice C.M. (2001) Curr Opin Infect Dis 14(6):743-7477; and Bartenschlager, R. (2002) Nature Reviews/Drug Discovery 1:911. An example of a useful *in vivo* host system for monitoring HCV antiviral efficacy is a chimeric human liver SCID mouse, as described by Mercer, *et al.* (2001) Nature Medicine 7(8):927-933.

It is furthermore proposed, without being limited by theory, that enhancement of T_H1 differentiation and/or suppression of T_H2 differentiation by IFN-alpha may be a contributing factor to interferon-alpha efficacy, for example, in the second phase of viral clearance. According to this theory, evolved IFN-alphas with increased potency in these biological activities (i.e., enhancement of T_H1 differentiation and/or suppression of T_H2 differentiation) would be predicted to have increased efficacy relative to, for example, currently approved therapeutic interferon-alpha molecules administered at the same dosage. An exemplary assay, described in the Examples section herein, monitors the enhancement of T_H1 differentiation and/or suppression of T_H2 differentiation by IFN-

alpha on naïve T_H0 cells, by measuring production of cytokines associated with the T_H1-phenotype (e.g., IFN-gamma) and/or the T_H2-phenotype (e.g., IL-5, IL4) via ELISA or via intracellular staining and FACS sorting.

The therapeutic efficacy of IFN-alpha molecules tends to be diminished in part due to dose-limiting toxicities, e.g. thrombocytopenia and neutropenia. Although the present invention is not intended to be limited by a particular theory of underlying mechanism, it is proposed that such toxicity may be associated with anti-proliferative effects of IFN-alpha on platelet and neutrophil precursors, and that antiproliferative activity in surrogate assay systems (such as those described herein) may be predictive of the relative toxicity of an interferon-alpha molecule. Thus, dose-limiting toxicities associated with IFN-alpha therapy may be diminished in IFN-alpha molecules that exhibit reduced antiproliferative activity relative to, for example, currently approved therapeutic interferon-alpha molecules, such as ROFERON®-A (Interferon alfa-2a, recombinant; Hoffmann-La Roche Inc.), INTRON® A (Interferon alfa-2b, recombinant; Schering Corporation), and INFERGEN® (interferon alfacon-1; InterMune, Inc.). An exemplary antiproliferative activity assay, described in the Examples section herein, monitors the effect of IFN-alpha on the proliferation of human Daudi lymphoid cells. Alternatively, or in addition, dose-limiting toxicities may be reduced as a result of administering more therapeutically active molecules, which would permit dosing in lower concentrations or at lower frequency than currently approved molecules.

It is an object of the invention to provide novel interferon-alpha polypeptides, and nucleic acids which encode the polypeptides. Polypeptides of the invention are useful for the treatment of diseases and disorders which are responsive to treatment by interferon-alpha, particularly diseases associated with viral infection, such as, for example, infection by HCV. Some polypeptides of the invention exhibit an interferon-alpha activity, such as, for example, antiviral activity, antiproliferative activity, and/or T_H1 differentiation activity. Some polypeptides of the invention exhibit one or more of the following properties: increased or decreased antiviral activity compared to a reference IFN-alpha polypeptide; increased or decreased T_H1 differentiation activity compared to a reference IFN-alpha polypeptide; increased or decreased antiproliferative activity compared to a reference IFN-alpha polypeptide. The reference IFN-alpha polypeptide may comprise a sequence of a non-naturally occurring interferon-alpha, such as IFN-alpha Con1 (SEQ ID

NO:333), or may comprise a sequence of a naturally-occurring (i.e., wild-type) interferon-alpha polypeptide. Examples of sequences of naturally occurring interferon-alpha polypeptides include sequences of human IFN-alpha polypeptides, such as, for example, huIFN-alpha 2b (SEQ ID NO:321), huIFN-alpha 2a (SEQ ID NO:322), huIFN-alpha 2c (SEQ ID NO:322 with position 34 = Arg), huIFN-alpha 8b (SEQ ID NO:327), huIFN-alpha 8a (SEQ ID NO:327 with positions 98 = Val, 99 = Leu, 100 = Cys, and 101 = Asp), huIFN-alpha 8c (SEQ ID NO:327 with position 161 = Asp and amino acids at positions 162-166 deleted), huIFN-alpha 14a (SEQ ID NO:329), huIFN-alpha 14c (SEQ ID NO:329 with position 152 = Leu), or a sequence of any other naturally occurring human interferon alpha polypeptide, such as those listed in Allen G. and Diaz M.O. (1996), *supra*.

In another aspect, the invention provides interferon-alpha polypeptides which exhibit enhanced efficacy in clearing a virus from virus-infected cells, compared to a reference interferon-alpha molecule, such as one currently employed as a therapeutic (such as, for example, ROFERON-A, INTRON A, or INFERGEN). Exemplary viruses include, but are not limited to, viruses of the *Flaviviridae* family, such as, for example, Hepatitis C Virus, Yellow Fever Virus, West Nile Virus, Japanese Encephalitis Virus, Dengue Virus, and Bovine Viral Diarrhea Virus; viruses of the *Hepadnaviridae* family, such as, for example, Hepatitis B Virus; viruses of the *Picornaviridae* family, such as, for example, Encephalomyocarditis Virus, Human Rhinovirus, and Hepatitis A Virus; viruses of the *Retroviridae* family, such as, for example, Human Immunodeficiency Virus, Simian Immunodeficiency Virus, Human T-Lymphotropic Virus, and Rous Sarcoma Virus; viruses of the *Coronaviridae* family, such as, for example, SARS coronavirus; viruses of the *Rhabdoviridae* family, such as, for example, Rabies Virus and Vesicular Stomatitis Virus, viruses of the *Paramyxoviridae* family, such as, for example, Respiratory Syncytial Virus and Parainfluenza Virus, viruses of the *Papillomaviridae* family, such as, for example, Human Papillomavirus, and viruses of the *Herpesviridae* family, such as, for example, Herpes Simplex Virus. Such enhanced efficacy may arise from enhanced antiviral activity, enhanced T_H1-differentiation activity, or both, relative to the reference molecule. For example, some interferon-alpha polypeptides of the invention may be particularly useful in clearing viruses or viral strains that show poor response to treatment

with interferon-alpha molecules currently in use, such as, for example, Genotype 1 of HCV.

Some polypeptides of the invention exhibit an increased ratio of (antiviral activity/antiproliferative activity) compared to the reference IFN-alpha molecule, and/or an increased ratio of (T_H1 differentiation activity/antiproliferative activity) compared to the reference IFN-alpha molecule. Polypeptides exhibiting such properties may be particularly effective in treatment of viral infections, such as, for example, infection by a virus listed above. Some such polypeptides may, for example, provide enhanced therapeutic efficacy over currently-approved interferon-alpha molecules in the treatment of HCV, in one or both phases of the biphasic viral clearance profile, and/or may exhibit reduced toxicity. Some such polypeptides may provide enhanced therapeutic efficacy over currently-approved interferon-alpha molecules in the treatment of Genotype 1 HCV.

It is another object of the invention to provide conjugates, such conjugates comprising one or more non-polypeptide moiety linked to a polypeptide of the invention, which conjugate exhibits an interferon-alpha activity (such as one or more of the activities listed above), and which optionally exhibits other desirable properties, such as increased serum half-life and/or functional *in vivo* half-life, and/or decreased antigenicity, compared to the non-conjugated polypeptide. Some such conjugates may exhibit enhanced efficacy in clearing a virus from cells infected with the virus, compared to a reference interferon-alpha molecule, such as an interferon-alpha conjugate currently employed as a therapeutic (such as, for example, PEGASYS® (Peginterferon alfa-2a; Hoffmann-La Roche, Inc.) or PEG-INTRON® (peginterferon alfa-2b; Schering Corporation). Exemplary viruses include, but are not limited to, viruses of the *Flaviviridae* family, such as, for example, Hepatitis C Virus, Yellow Fever Virus, West Nile Virus, Japanese Encephalitis Virus, Dengue Virus, and Bovine Viral Diarrhea Virus; viruses of the *Hepadnaviridae* family, such as, for example, Hepatitis B Virus; viruses of the *Picornaviridae* family, such as, for example, Encephalomyocarditis Virus, Human Rhinovirus, and Hepatitis A Virus; viruses of the *Retroviridae* family, such as, for example, Human Immunodeficiency Virus, Simian Immunodeficiency Virus, Human T-Lymphotropic Virus, and Rous Sarcoma Virus; viruses of the *Coronaviridae* family, such as, for example, SARS coronavirus; viruses of the *Rhabdoviridae* family, such as, for example, Rabies Virus and Vesicular Stomatitis Virus, viruses of the *Paramyxoviridae*

family, such as, for example, Respiratory Syncytial Virus and Parainfluenza Virus, viruses of the *Papillomaviridae* family, such as, for example, Human Papillomavirus, and viruses of the *Herpesviridae* family, such as, for example, Herpes Simplex Virus. Such enhanced efficacy may arise from enhanced antiviral activity, enhanced T_H1-differentiation activity, or both, relative to the reference molecule. For example, some interferon-alpha conjugates of the invention may be particularly useful in clearing viruses or viral strains that show poor response to treatment with interferon-alpha molecules currently in use, such as, for example, Genotype 1 of HCV.

Some conjugates of the invention exhibit an increased ratio of (antiviral activity/antiproliferative activity) compared to the reference IFN-alpha molecule, and/or an increased ratio of (T_H1 differentiation activity/antiproliferative activity) compared to the reference IFN-alpha molecule. Conjugates exhibiting such properties may be particularly effective in treatment of viral infections, such as infection by a virus listed above, such as, for example, HCV. Some such conjugates may, for example, provide enhanced therapeutic efficacy over currently-approved interferon-alpha molecules in the treatment of HCV, in one or both phases of the biphasic viral clearance profile, and/or may exhibit reduced toxicity. Some such conjugates may provide enhanced therapeutic efficacy over currently-approved interferon-alpha molecules in the treatment of Genotype 1 HCV.

It is another object of the invention to provide a method of inhibiting viral replication in virus-infected cells, the method comprising administering to the virus-infected cells a polypeptide or conjugate of the invention in an amount effective to inhibit viral replication in said cells. The invention also provides a method of reducing the number of copies of a virus in virus-infected cells, comprising administering to the virus-infected cells a polypeptide or conjugate of the invention in an amount effective to reduce the number of copies of the virus in said cells. The virus may be a virus of the *Flaviviridae* family, such as, for example, Hepatitis C Virus, Yellow Fever Virus, West Nile Virus, Japanese Encephalitis Virus, Dengue Virus, or Bovine Viral Diarrhea Virus; a virus of the *Hepadnaviridae* family, such as, for example, Hepatitis B Virus; a virus of the *Picornaviridae* family, such as, for example, Encephalomyocarditis Virus, Human Rhinovirus, or Hepatitis A Virus; a virus of the *Retroviridae* family, such as, for example, Human Immunodeficiency Virus, Simian Immunodeficiency Virus, Human T-

Lymphotropic Virus, or Rous Sarcoma Virus; a virus of the *Coronaviridae* family, such as, for example, SARS coronavirus; a virus of the *Rhabdoviridae* family, such as, for example, Rabies Virus or Vesicular Stomatitis Virus; a virus of the *Paramyxoviridae* family, such as, for example, Respiratory Syncytial Virus or Parainfluenza Virus; a virus of the *Papillomaviridae* family, such as, for example, Human Papillomavirus; or a virus of the *Herpesviridae* family, such as, for example, Herpes Simplex Virus. The virus may for example be an RNA virus, such as HCV, a DNA virus, such as HBV, or a retrovirus, such as HIV. The cells may be in culture or otherwise isolated from a mammal (i.e., *in vitro* or *ex vivo*), or may be *in vivo*, e.g., in a mammal (e.g. such as a SCID mouse model as described by Mercer, *et al.* (2001) Nature Medicine. 7(8): 927-933), in a primate, or in man.

The invention also provides a method of enhancing T_H1 differentiation of T_H0 cells, comprising administering to a population comprising T_H0 cells a polypeptide or conjugate of the invention in an amount effective to increase the production of a cytokine associated with the T_H1-phenotype (e.g., IFN-gamma) and/or decrease the production of a cytokine associated with the T_H2-phenotype (e.g., IL-4 or IL-5) in said population. The population may be in culture or otherwise isolated from a mammal (i.e., *in vitro* or *ex vivo*), or may be *in vivo*, e.g., in a mammal, in a primate, or in man.

The invention also provides a method of inhibiting proliferation of a cell population, comprising contacting the cell population with a polypeptide, variant, or conjugate of the invention in an amount effective to decrease proliferation of the cell population. The cell population may be in culture or otherwise isolated from a mammal (i.e., *in vitro* or *ex vivo*), or may be *in vivo*, e.g., in a mammal, a primate, or man.

These and other objects of the invention are discussed in more detail below.

POLYPEPTIDES OF THE INVENTION

The invention provides novel interferon-alpha polypeptides, collectively referred to herein as "polypeptides of the invention". The term "polypeptide(s) of the invention" is intended throughout to include variants of the polypeptide sequences disclosed herein. Also included in this invention are fusion proteins comprising polypeptides of the invention, and conjugates comprising polypeptides of the invention.

Fragments of human interferon-alpha nucleic acids were recursively recombined to form libraries of shufflants comprising recombinant polynucleotides, from which

polypeptides of the invention were derived. Methods for obtaining libraries of recombinant polynucleotides and/or for obtaining diversity in nucleic acids used as the substrates for recursive sequence recombination are described *infra*.

Exemplary polypeptides of the invention include polypeptides comprising the sequences identified herein as SEQ ID NO:1-SEQ ID NO:319 (i.e., SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID

NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, SEQ ID NO:242, SEQ ID NO:243, SEQ ID NO:244, SEQ ID NO:245, SEQ ID NO:246, SEQ ID NO:247, SEQ ID NO:248, SEQ ID NO:249, SEQ ID NO:250, SEQ ID NO:251, SEQ ID NO:252, SEQ ID NO:253, SEQ ID NO:254, SEQ ID NO:255, SEQ ID NO:256, SEQ ID NO:257, SEQ ID NO:258, SEQ ID NO:259, SEQ ID NO:260, SEQ ID NO:261, SEQ ID NO:262, SEQ ID NO:263, SEQ ID NO:264, SEQ ID NO:265, SEQ ID NO:266, SEQ ID NO:267, SEQ ID NO:268, SEQ ID NO:269, SEQ ID NO:270, SEQ ID NO:271, SEQ ID NO:272, SEQ ID NO:273, SEQ ID NO:274, SEQ ID NO:275, SEQ ID NO:276, SEQ ID NO:277, SEQ ID NO:278, SEQ ID NO:279, SEQ ID NO:280, SEQ ID NO:281, SEQ ID NO:282, SEQ ID NO:283, SEQ ID NO:284, SEQ ID NO:285, SEQ ID NO:286, SEQ ID NO:287, SEQ ID NO:288, SEQ ID NO:289, SEQ ID NO:290, SEQ ID NO:291, SEQ ID NO:292, SEQ ID NO:293, SEQ ID NO:294, SEQ ID NO:295, SEQ ID NO:296, SEQ ID NO:297, SEQ ID

NO:298, SEQ ID NO:299, SEQ ID NO:300, SEQ ID NO:301, SEQ ID NO:302, SEQ ID NO:303, SEQ ID NO:304, SEQ ID NO:305, SEQ ID NO:306, SEQ ID NO:307, SEQ ID NO:308, SEQ ID NO:309, SEQ ID NO:310, SEQ ID NO:311, SEQ ID NO:312, SEQ ID NO:313, SEQ ID NO:314, SEQ ID NO:315, SEQ ID NO:316, SEQ ID NO:317, SEQ ID NO:318, and SEQ ID NO:319), shown in Figures 6A-6V. Such polypeptides exhibit an interferon-alpha activity, including antiviral activity in a HeLa/EMCV antiviral assay. The polypeptides may further comprise one or more additional amino acid(s), such as, for example, a methionine added to the N-terminus. The invention also provides fusion proteins and conjugates comprising these polypeptides, and isolated or recombinant nucleic acids encoding these polypeptides.

The invention also includes isolated or recombinant polypeptides which each comprise a sequence which differs in 0 to 16 amino acid positions from a sequence selected from SEQ ID NO:1 - SEQ ID NO:319, e.g., differs in 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, or 16 amino acid positions, e.g., differs in 0-16 amino acid positions, 0-15 amino acid positions, in 0-14 amino acid positions, in 0-13 amino acid positions, in 0-12 amino acid positions, 0-11 amino acid positions, in 0-10 amino acid positions, in 0-9 amino acid positions, in 0-8 amino acid positions, in 0-7 amino acid positions, in 0-6 amino acid positions, in 0-5 amino acid positions, in 0-4 amino acid positions, in 0-3 amino acid positions, in 0-2 amino acid positions or in 0-1 amino acid positions. Some such polypeptides comprise a sequence which differs in 0 to 16 amino acid positions from a sequence selected from SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:18, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:30, SEQ ID NO:46, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:94, SEQ ID NO:103, SEQ ID NO:107, SEQ ID NO:124, SEQ ID NO:127, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:148, SEQ ID NO:167, SEQ ID NO:171, SEQ ID NO:176, SEQ ID NO:179, SEQ ID NO:191, SEQ ID NO:195, SEQ ID NO:208, SEQ ID NO:232, SEQ ID NO:234, SEQ ID NO:258, SEQ ID NO:260, SEQ ID NO:262, SEQ ID NO:263, SEQ ID NO:266, SEQ ID NO:293, SEQ ID NO:296, SEQ ID NO:297, SEQ ID NO:298, SEQ ID NO:303, SEQ ID NO:306, SEQ ID NO:310, and SEQ ID NO:312.

The invention also includes isolated or recombinant polypeptides which each comprise a sequence which differs in 0 to 16 amino acid positions from a sequence

selected from SEQ ID NO:312 (M01); SEQ ID NO:262 (M04); SEQ ID NO:266 (M05); SEQ ID NO:232 (M23); SEQ ID NO:88 (M45); SEQ ID NO:297 (M20); SEQ ID NO:167 (M27); SEQ ID NO:107 (M09); SEQ ID NO:208 (M02); SEQ ID NO:94 (M33); SEQ ID NO:141 (M37); SEQ ID NO:46 (M30); SEQ ID NO:171 (M22); SEQ ID NO:310 (M24); SEQ ID NO:176 (M44); SEQ ID NO:26 (M31); SEQ ID NO:89 (M10); SEQ ID NO:296 (M14); SEQ ID NO:148 (M03); SEQ ID NO:18 (M46); SEQ ID NO:10 (M26); SEQ ID NO:87 (M21); SEQ ID NO:103 (M38); SEQ ID NO:234 (M28); SEQ ID NO:30 (M19); SEQ ID NO:179 (M11); SEQ ID NO:2 (M34); SEQ ID NO:260 (M07); SEQ ID NO:306 (M18); SEQ ID NO:140 (M40); SEQ ID NO:127 (M16); SEQ ID NO:293 (M25); SEQ ID NO:195 (M29); SEQ ID NO:191 (M36); SEQ ID NO:263 (M06); SEQ ID NO:1 (M32); SEQ ID NO:298 (M39); SEQ ID NO:24 (M42); SEQ ID NO:258 (M08); SEQ ID NO:124 (M35); SEQ ID NO:7 (M41); SEQ ID NO:9 (M12); SEQ ID NO:303 (M17); and SEQ ID NO:6 (M43); e.g., differs in 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, or 16 amino acid positions, e.g., differs in 0-16 amino acid positions, 0-15 amino acid positions, in 0-14 amino acid positions, in 0-13 amino acid positions, in 0-12 amino acid positions, 0-11 amino acid positions, in 0-10 amino acid positions, in 0-9 amino acid positions, in 0-8 amino acid positions, in 0-7 amino acid positions, in 0-6 amino acid positions, in 0-5 amino acid positions, in 0-4 amino acid positions, in 0-3 amino acid positions, in 0-2 amino acid positions or in 0-1 amino acid positions, such as, for example, polypeptides described below. Some such polypeptides exhibit an interferon-alpha activity (such as, e.g., antiviral activity, T_H1 differentiation activity, and/or antiproliferative activity). Some such polypeptides exhibit at least two fold greater antiviral activity than human IFN-alpha 2a in a HeLa/EMCV antiviral assay. Some such polypeptides bind to the human interferon-alpha receptor with a higher affinity (lower EC_{50}) than that of IFN-alpha 2a. The polypeptides may further comprise one or more additional amino acid(s), such as, for example, a methionine added to the N-terminus. The invention also provides fusion proteins and conjugates comprising these polypeptides, and isolated or recombinant nucleic acids encoding these polypeptides.

The invention includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 8 amino acid positions from the sequence SEQ ID NO:1 (clone M32), that is, comprises a sequence which is at least 95% identical to SEQ ID NO:1, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide

comprising the sequence SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:18, SEQ ID NO:44, SEQ ID NO:69, SEQ ID NO:116, SEQ ID NO:163, SEQ ID NO:201, SEQ ID NO:207, SEQ ID NO:247, SEQ ID NO:255, SEQ ID NO:260, SEQ ID NO:290, or SEQ ID NO:302. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 6 amino acid positions from the sequence SEQ ID NO:1, that is, comprises a sequence which is at least 96% identical to SEQ ID NO:1, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:18, SEQ ID NO:44, SEQ ID NO:260, or SEQ ID NO:302. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 3 amino acid positions from the sequence SEQ ID NO:1, that is, comprises a sequence which is at least 98% identical to SEQ ID NO:1, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:1, SEQ ID NO:18, or SEQ ID NO:44.

The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 8 amino acid positions from the sequence SEQ ID NO:2 (clone M34), that is, comprises a sequence which is at least 95% identical to SEQ ID NO:2, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:11, SEQ ID NO:16, SEQ ID NO:21, SEQ ID NO:26, SEQ ID NO:29, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:48, SEQ ID NO:49, or SEQ ID NO:293. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 6 amino acid positions from the sequence SEQ ID NO:2 , that is, comprises a sequence which is at least 96% identical to SEQ ID NO:2, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:11, SEQ ID NO:21, SEQ ID NO:42, SEQ ID NO:49, or SEQ ID NO:293. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 3 amino acid positions from the sequence SEQ ID NO:2, that is, comprises a sequence which is at least 98% identical to SEQ ID NO:2, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the

sequence SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:11, SEQ ID NO:21, SEQ ID NO:49, or SEQ ID NO:293.

The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 8 amino acid positions from the sequence SEQ ID NO:6 (clone M43), that is, comprises a sequence which is at least 95% identical to SEQ ID NO:6, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:11, SEQ ID NO:16, SEQ ID NO:21, SEQ ID NO:26, SEQ ID NO:29, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:48, SEQ ID NO:49, or SEQ ID NO:293. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 6 amino acid positions from the sequence SEQ ID NO:6, that is, comprises a sequence which is at least 96% identical to SEQ ID NO:6, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:11, SEQ ID NO:21, SEQ ID NO:42, SEQ ID NO:48, SEQ ID NO:49, or SEQ ID NO:293. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 3 amino acid positions from the sequence SEQ ID NO:6 , that is, comprises a sequence which is at least 98% identical to SEQ ID NO:6, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:11, SEQ ID NO:21, SEQ ID NO:49, or SEQ ID NO:293.

The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 8 amino acid positions from the sequence SEQ ID NO:7 (clone M41), that is, comprises a sequence which is at least 95% identical to SEQ ID NO:7, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:7, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:37, or SEQ ID NO:313. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 6 amino acid positions from the sequence SEQ ID NO:7 , that is, comprises a sequence which is at least 96% identical to SEQ ID NO:7, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:7, SEQ ID NO:25, SEQ ID NO:37, or SEQ ID NO:313. The invention also includes an isolated or recombinant

polypeptide which comprises a sequence which differs in 0 to 3 amino acid positions from the sequence SEQ ID NO:7, that is, comprises a sequence which is at least 98% identical to SEQ ID NO:7, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:7 or SEQ ID NO:313.

The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 8 amino acid positions from the sequence SEQ ID NO:9 (clone M12), that is, comprises a sequence which is at least 95% identical to SEQ ID NO:9, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:9, SEQ ID NO:13, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:38, SEQ ID NO:41, SEQ ID NO:45, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:73, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:224, SEQ ID NO:231, SEQ ID NO:238, SEQ ID NO:240, SEQ ID NO:294, or SEQ ID NO:305. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 6 amino acid positions from the sequence SEQ ID NO:9, that is, comprises a sequence which is at least 96% identical to SEQ ID NO:9, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:9, SEQ ID NO:13, SEQ ID NO:35, SEQ ID NO:38, SEQ ID NO:41, SEQ ID NO:45, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:73, SEQ ID NO:221, SEQ ID NO:238, SEQ ID NO:240, SEQ ID NO:294, or SEQ ID NO:305.

The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 8 amino acid positions from the sequence SEQ ID NO:10 (clone M26), that is, comprises a sequence which is at least 95% identical to SEQ ID NO:10, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:5, SEQ ID NO:10, SEQ ID NO:23, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:36, SEQ ID NO:47, SEQ ID NO:71, SEQ ID NO:205, SEQ ID NO:230, SEQ ID NO:306, or SEQ ID NO:308. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 6 amino acid positions from the sequence SEQ ID NO:10, that is, comprises a sequence which is at least 96% identical to SEQ ID NO:10, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the

sequence SEQ ID NO:10, SEQ ID NO:23, SEQ ID NO:47, SEQ ID NO:205, or SEQ ID NO:230.

In another aspect, the invention includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 8 amino acid positions from the sequence SEQ ID NO:18 (clone M46), that is, comprises a sequence which is at least 95% identical to SEQ ID NO:18, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:18, SEQ ID NO:44, SEQ ID NO:69, SEQ ID NO:109, SEQ ID NO:113, SEQ ID NO:116, SEQ ID NO:145, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:184, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:201, SEQ ID NO:207, SEQ ID NO:218, SEQ ID NO:237, SEQ ID NO:247, SEQ ID NO:255, SEQ ID NO:260, SEQ ID NO:270, SEQ ID NO:276, SEQ ID NO:283, SEQ ID NO:290, or SEQ ID NO:302. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 6 amino acid positions from the sequence SEQ ID NO:18, that is, comprises a sequence which is at least 96% identical to SEQ ID NO:18, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:18, SEQ ID NO:44, SEQ ID NO:116, SEQ ID NO:201, SEQ ID NO:207, SEQ ID NO:255, SEQ ID NO:260, SEQ ID NO:290, or SEQ ID NO:302. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 3 amino acid positions from the sequence SEQ ID NO:18, that is, comprises a sequence which is at least 98% identical to SEQ ID NO:18, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:1, SEQ ID NO:18, SEQ ID NO:44, or SEQ ID NO:260.

In another aspect, the invention includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 8 amino acid positions from the sequence SEQ ID NO:24 (clone M42), that is, comprises a sequence which is at least 95% identical to SEQ ID NO:24, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:7, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:28, SEQ ID NO:32, or SEQ ID NO:43. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 6 amino acid positions from the sequence SEQ ID NO:24, that is,

comprises a sequence which is at least 96% identical to SEQ ID NO:24, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:24, or SEQ ID NO:32.

The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 8 amino acid positions from the sequence SEQ ID NO:26 (clone M31), that is, comprises a sequence which is at least 95% identical to SEQ ID NO:26, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:11, SEQ ID NO:16, SEQ ID NO:21, SEQ ID NO:26, SEQ ID NO:29, SEQ ID NO:42, SEQ ID NO:49, or SEQ ID NO:293. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 6 amino acid positions from the sequence SEQ ID NO:26, that is, comprises a sequence which is at least 96% identical to SEQ ID NO:26, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:26, SEQ ID NO:29, SEQ ID NO:42, or SEQ ID NO:293.

The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 8 amino acid positions from the sequence SEQ ID NO:30 (clone M19), that is, comprises a sequence which is at least 95% identical to SEQ ID NO:30, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:10, SEQ ID NO:30, SEQ ID NO:40, or SEQ ID NO:71. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 6 amino acid positions from the sequence SEQ ID NO:30 , that is, comprises a sequence which is at least 96% identical to SEQ ID NO:30, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:30 or SEQ ID NO:71.

The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 8 amino acid positions from the sequence SEQ ID NO:46 (clone M30), that is, comprises a sequence which is at least 95% identical to SEQ ID NO:46, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:39, SEQ ID NO:46, SEQ ID NO:77, SEQ ID NO:213, SEQ ID NO:216, SEQ ID NO:239, SEQ ID NO:241, SEQ ID NO:243, SEQ ID NO:250, SEQ ID NO:264, SEQ ID NO:297, SEQ ID NO:304, SEQ ID NO:310,

or SEQ ID NO:312. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 6 amino acid positions from the sequence SEQ ID NO:46, that is, comprises a sequence which is at least 96% identical to SEQ ID NO:46, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:39, SEQ ID NO:46, SEQ ID NO:77, SEQ ID NO:241, SEQ ID NO:250, SEQ ID NO:310, or SEQ ID NO:312.

The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 8 amino acid positions from the sequence SEQ ID NO:87 (clone M21), that is, comprises a sequence which is at least 95% identical to SEQ ID NO:87, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:87, SEQ ID NO:261, or SEQ ID NO:299.

The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 8 amino acid positions from the sequence SEQ ID NO:88 (clone M45), that is, comprises a sequence which is at least 95% identical to SEQ ID NO:88, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:66, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:88, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:103, SEQ ID NO:113, SEQ ID NO:117, SEQ ID NO:120, SEQ ID NO:124, SEQ ID NO:145, SEQ ID NO:149, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:199, SEQ ID NO:202, SEQ ID NO:223, SEQ ID NO:284, SEQ ID NO:288, SEQ ID NO:289, SEQ ID NO:290, SEQ ID NO:295, SEQ ID NO:296, or SEQ ID NO:314. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 6 amino acid positions from the sequence SEQ ID NO:88, that is, comprises a sequence which is at least 96% identical to SEQ ID NO:88, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:66, SEQ ID NO:84, SEQ ID NO:88, SEQ ID NO:91, SEQ ID NO:113, SEQ ID NO:117, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:199, SEQ ID NO:284, SEQ ID NO:288, SEQ ID NO:290, SEQ ID NO:295, SEQ ID NO:296, or SEQ ID NO:314. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 3 amino acid positions from the sequence SEQ ID NO:88, that is, comprises a sequence which is at least 98% identical to SEQ ID NO:88, and which

exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:88 or SEQ ID NO:288.

The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 8 amino acid positions from the sequence SEQ ID NO:89 (clone M10), that is, comprises a sequence which is at least 95% identical to SEQ ID NO:89, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:89 or SEQ ID NO:298.

The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 8 amino acid positions from the sequence SEQ ID NO:94 (clone M33), that is, comprises a sequence which is at least 95% identical to SEQ ID NO:94, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:57, SEQ ID NO:94, SEQ ID NO:237, SEQ ID NO:255, or SEQ ID NO:273.

The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 8 amino acid positions from the sequence SEQ ID NO:103 (clone M38), that is, comprises a sequence which is at least 95% identical to SEQ ID NO:103, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:58, SEQ ID NO:85, SEQ ID NO:88, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:113, SEQ ID NO:117, SEQ ID NO:120, SEQ ID NO:124, SEQ ID NO:128, SEQ ID NO:145, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:184, SEQ ID NO:199, SEQ ID NO:223, SEQ ID NO:244, SEQ ID NO:276, SEQ ID NO:283, SEQ ID NO:284, SEQ ID NO:290, SEQ ID NO:295, SEQ ID NO:296, SEQ ID NO:309, or SEQ ID NO:314. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 6 amino acid positions from the sequence SEQ ID NO:103, that is, comprises a sequence which is at least 96% identical to SEQ ID NO:103, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:58, SEQ ID NO:85, SEQ ID NO:93, SEQ ID NO:98, SEQ ID NO:103, SEQ ID NO:113, SEQ ID NO:120, SEQ ID NO:124, SEQ ID NO:128, SEQ ID NO:145, SEQ ID NO:184, SEQ ID NO:199, SEQ ID NO:290, SEQ ID NO:295, SEQ ID NO:296, SEQ ID NO:309, or SEQ ID NO:314. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which

differs in 0 to 3 amino acid positions from the sequence SEQ ID NO:103, that is, comprises a sequence which is at least 98% identical to SEQ ID NO:103, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:58, SEQ ID NO:85, SEQ ID NO:103, SEQ ID NO:113, SEQ ID NO:120, SEQ ID NO:124, SEQ ID NO:145, SEQ ID NO:199, SEQ ID NO:295, or SEQ ID NO:296.

The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 8 amino acid positions from the sequence SEQ ID NO:107 (clone M9), that is, comprises a sequence which is at least 95% identical to SEQ ID NO:107, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:107 or SEQ ID NO:301.

The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 8 amino acid positions from the sequence SEQ ID NO:124 (clone M35), that is, comprises a sequence which is at least 95% identical to SEQ ID NO:124, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:58, SEQ ID NO:85, SEQ ID NO:88, SEQ ID NO:93, SEQ ID NO:98, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:117, SEQ ID NO:120, SEQ ID NO:124, SEQ ID NO:128, SEQ ID NO:145, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:184, SEQ ID NO:199, SEQ ID NO:290, SEQ ID NO:295, SEQ ID NO:296, SEQ ID NO:309, or SEQ ID NO:314. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 6 amino acid positions from the sequence SEQ ID NO:124, that is, comprises a sequence which is at least 96% identical to SEQ ID NO:124, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:85, SEQ ID NO:93, SEQ ID NO:98, SEQ ID NO:103, SEQ ID NO:113, SEQ ID NO:120, SEQ ID NO:124, SEQ ID NO:128, SEQ ID NO:145, SEQ ID NO:199, SEQ ID NO:290, SEQ ID NO:295, SEQ ID NO:296, or SEQ ID NO:314. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 3 amino acid positions from the sequence SEQ ID NO:124, that is, comprises a sequence which is at least 98% identical to SEQ ID NO:124, and which exhibits an interferon-alpha activity; such as, for example,

a polypeptide comprising the sequence SEQ ID NO:98, SEQ ID NO:103, SEQ ID NO:113, SEQ ID NO:120, SEQ ID NO:124, SEQ ID NO:145, or SEQ ID NO:295.

The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 8 amino acid positions from the sequence SEQ ID NO:127 (clone M16), that is, comprises a sequence which is at least 95% identical to SEQ ID NO:127, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:127, SEQ ID NO:197, SEQ ID NO:261, or SEQ ID NO:268.

The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 8 amino acid positions from the sequence SEQ ID NO:140 (clone M40), that is, comprises a sequence which is at least 95% identical to SEQ ID NO:140, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:108, SEQ ID NO:140, SEQ ID NO:272, or SEQ ID NO:278.

The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 8 amino acid positions from the sequence SEQ ID NO:141 (clone M37), that is, comprises a sequence which is at least 95% identical to SEQ ID NO:141, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:141 or SEQ ID NO:160.

The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 8 amino acid positions from the sequence SEQ ID NO:148 (clone M3) that is, comprises a sequence which is at least 95% identical to SEQ ID NO:148, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:148, SEQ ID NO:170, or SEQ ID NO:206. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 6 amino acid positions from the sequence SEQ ID NO:148, that is, comprises a sequence which is at least 96% identical to SEQ ID NO:148, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:148 or SEQ ID NO:170.

The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 8 amino acid positions from the sequence SEQ ID NO:167 (clone M27), that is, comprises a sequence which is at least 95% identical to

SEQ ID NO:167, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:65, SEQ ID NO:102, SEQ ID NO:118, SEQ ID NO:143, SEQ ID NO:159, SEQ ID NO:167, SEQ ID NO:181, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:271, or SEQ ID NO:315. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 6 amino acid positions from the sequence SEQ ID NO:167, that is, comprises a sequence which is at least 96% identical to SEQ ID NO:167, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:159, SEQ ID NO:167, SEQ ID NO:181, or SEQ ID NO:315. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 3 amino acid positions from the sequence SEQ ID NO:167, that is, comprises a sequence which is at least 98% identical to SEQ ID NO:167, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:159, SEQ ID NO:167, SEQ ID NO:181, or SEQ ID NO:315.

The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 8 amino acid positions from the sequence SEQ ID NO:191 (clone M36), that is, comprises a sequence which is at least 95% identical to SEQ ID NO:191, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:133 or SEQ ID NO:191.

The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 8 amino acid positions from the sequence SEQ ID NO:195 (clone M29), that is, comprises a sequence which is at least 95% identical to SEQ ID NO:195, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:105, SEQ ID NO:108, SEQ ID NO:131, SEQ ID NO:137, SEQ ID NO:150, SEQ ID NO:195, SEQ ID NO:234, or SEQ ID NO:278. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 6 amino acid positions from the sequence SEQ ID NO:195, that is, comprises a sequence which is at least 96% identical to SEQ ID NO:195, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:108, SEQ ID NO:195, or SEQ ID NO:278. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which

differs in 0 to 3 amino acid positions from the sequence SEQ ID NO:195, that is, comprises a sequence which is at least 98% identical to SEQ ID NO:195, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:195 or SEQ ID NO:278.

The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 8 amino acid positions from the sequence SEQ ID NO:208 (clone M02), that is, comprises a sequence which is at least 95% identical to SEQ ID NO:208, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:67 or SEQ ID NO:208.

The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 8 amino acid positions from the sequence SEQ ID NO:232 (clone M23), that is, comprises a sequence which is at least 95% identical to SEQ ID NO:232, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:12, SEQ ID NO:167, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:262, or SEQ ID NO:312. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 6 amino acid positions from the sequence SEQ ID NO:232, that is, comprises a sequence which is at least 96% identical to SEQ ID NO:232, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:232 or SEQ ID NO:262.

The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 8 amino acid positions from the sequence SEQ ID NO:234 (clone M28), that is, comprises a sequence which is at least 95% identical to SEQ ID NO:234, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:105, SEQ ID NO:139, SEQ ID NO:188, SEQ ID NO:195, SEQ ID NO:234, SEQ ID NO:278, or SEQ ID NO:285. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 6 amino acid positions from the sequence SEQ ID NO:234, that is, comprises a sequence which is at least 96% identical to SEQ ID NO:234, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:105, SEQ ID NO:139, SEQ ID NO:234, SEQ ID NO:278, or SEQ ID NO:285. The invention also includes an isolated or recombinant

polypeptide which comprises a sequence which differs in 0 to 3 amino acid positions from the sequence SEQ ID NO:234, that is, comprises a sequence which is at least 98% identical to SEQ ID NO:234, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:105 or SEQ ID NO:234.

The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 8 amino acid positions from the sequence SEQ ID NO:258 (clone M8), that is, comprises a sequence which is at least 95% identical to SEQ ID NO:258, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:99 or SEQ ID NO:258.

The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 8 amino acid positions from the sequence SEQ ID NO:260 (clone M07), that is, comprises a sequence which is at least 95% identical to SEQ ID NO:260, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:18, SEQ ID NO:44, SEQ ID NO:69, SEQ ID NO:109, SEQ ID NO:113, SEQ ID NO:116, SEQ ID NO:145, SEQ ID NO:161, SEQ ID NO:163, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:184, SEQ ID NO:188, SEQ ID NO:201, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:218, SEQ ID NO:228, SEQ ID NO:237, SEQ ID NO:247, SEQ ID NO:255, SEQ ID NO:257, SEQ ID NO:260, SEQ ID NO:276, or SEQ ID NO:290. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 6 amino acid positions from the sequence SEQ ID NO:260, that is, comprises a sequence which is at least 96% identical to SEQ ID NO:260, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:18, SEQ ID NO:44, SEQ ID NO:69, SEQ ID NO:116, SEQ ID NO:201, SEQ ID NO:207, SEQ ID NO:247, SEQ ID NO:255, SEQ ID NO:260, or SEQ ID NO:290. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 3 amino acid positions from the sequence SEQ ID NO:260, that is, comprises a sequence which is at least 98% identical to SEQ ID NO:260, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:18 or SEQ ID NO:260.

The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 8 amino acid positions from the sequence SEQ ID NO:262 (clone M04), that is, comprises a sequence which is at least 95% identical to SEQ ID NO:262, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:12, SEQ ID NO:39, SEQ ID NO:77, SEQ ID NO:216, SEQ ID NO:232, SEQ ID NO:239, SEQ ID NO:241, SEQ ID NO:243, SEQ ID NO:250, SEQ ID NO:262, SEQ ID NO:264, SEQ ID NO:297, SEQ ID NO:304, SEQ ID NO:310, or SEQ ID NO:312. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 6 amino acid positions from the sequence SEQ ID NO:262, that is, comprises a sequence which is at least 96% identical to SEQ ID NO:262, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:12, SEQ ID NO:77, SEQ ID NO:216, SEQ ID NO:232, SEQ ID NO:241, SEQ ID NO:243, SEQ ID NO:250, SEQ ID NO:262, SEQ ID NO:264, SEQ ID NO:297, SEQ ID NO:304, SEQ ID NO:310, or SEQ ID NO:312.

The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 8 amino acid positions from the sequence SEQ ID NO:266 (clone M05), that is, comprises a sequence which is at least 95% identical to SEQ ID NO:266, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:79, SEQ ID NO:90, SEQ ID NO:114, SEQ ID NO:215, SEQ ID NO:229, SEQ ID NO:245, SEQ ID NO:266, or SEQ ID NO:274. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 6 amino acid positions from the sequence SEQ ID NO:266, that is, comprises a sequence which is at least 96% identical to SEQ ID NO:266, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:79, SEQ ID NO:90, SEQ ID NO:215, SEQ ID NO:229, SEQ ID NO:245, SEQ ID NO:266, or SEQ ID NO:274.

The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 8 amino acid positions from the sequence SEQ ID NO:293 (clone M25), that is, comprises a sequence which is at least 95% identical to SEQ ID NO:293, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ

ID NO:8, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:16, SEQ ID NO:21, SEQ ID NO:26, SEQ ID NO:29, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:48, SEQ ID NO:49, or SEQ ID NO:293. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 6 amino acid positions from the sequence SEQ ID NO:293, that is, comprises a sequence which is at least 96% identical to SEQ ID NO:293, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:11, SEQ ID NO:21, SEQ ID NO:26, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:49, or SEQ ID NO:293. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 3 amino acid positions from the sequence SEQ ID NO:293, that is, comprises a sequence which is at least 98% identical to SEQ ID NO:293, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:11, SEQ ID NO:21, SEQ ID NO:49, or SEQ ID NO:293.

The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 8 amino acid positions from the sequence SEQ ID NO:296 (clone M14), that is, comprises a sequence which is at least 95% identical to SEQ ID NO:296, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:58, SEQ ID NO:66, SEQ ID NO:85, SEQ ID NO:88, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:113, SEQ ID NO:117, SEQ ID NO:120, SEQ ID NO:124, SEQ ID NO:128, SEQ ID NO:145, SEQ ID NO:149, SEQ ID NO:151, SEQ ID NO:184, SEQ ID NO:199, SEQ ID NO:202, SEQ ID NO:223, SEQ ID NO:244, SEQ ID NO:284, SEQ ID NO:288, SEQ ID NO:290, SEQ ID NO:295, SEQ ID NO:296, SEQ ID NO:309, or SEQ ID NO:314. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 6 amino acid positions from the sequence SEQ ID NO:296, that is, comprises a sequence which is at least 96% identical to SEQ ID NO:296, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:58, SEQ ID NO:85, SEQ ID NO:88, SEQ ID NO:93, SEQ ID NO:98, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:113, SEQ ID NO:117, SEQ ID NO:120, SEQ ID NO:124, SEQ ID NO:145, SEQ ID

NO:184, SEQ ID NO:199, SEQ ID NO:284, SEQ ID NO:290, SEQ ID NO:295, SEQ ID NO:296, SEQ ID NO:309, or SEQ ID NO:314. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 3 amino acid positions from the sequence SEQ ID NO:296, that is, comprises a sequence which is at least 98% identical to SEQ ID NO:296, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:103, SEQ ID NO:113, SEQ ID NO:145, SEQ ID NO:184, SEQ ID NO:199, SEQ ID NO:290, SEQ ID NO:295, SEQ ID NO:296, or SEQ ID NO:314.

The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 8 amino acid positions from the sequence SEQ ID NO:297 (clone M20), that is, comprises a sequence which is at least 95% identical to SEQ ID NO:297, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:12, SEQ ID NO:39, SEQ ID NO:46, SEQ ID NO:77, SEQ ID NO:216, SEQ ID NO:239, SEQ ID NO:241, SEQ ID NO:243, SEQ ID NO:250, SEQ ID NO:262, SEQ ID NO:264, SEQ ID NO:297, SEQ ID NO:304, SEQ ID NO:310, or SEQ ID NO:312. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 6 amino acid positions from the sequence SEQ ID NO:297, that is, comprises a sequence which is at least 96% identical to SEQ ID NO:297, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:12, SEQ ID NO:39, SEQ ID NO:77, SEQ ID NO:216, SEQ ID NO:239, SEQ ID NO:241, SEQ ID NO:243, SEQ ID NO:250, SEQ ID NO:262, SEQ ID NO:264, SEQ ID NO:297, SEQ ID NO:304, SEQ ID NO:310, or SEQ ID NO:312. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 3 amino acid positions from the sequence SEQ ID NO:297, that is, comprises a sequence which is at least 98% identical to SEQ ID NO:297, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:77, SEQ ID NO:216, SEQ ID NO:241, SEQ ID NO:243, SEQ ID NO:250, SEQ ID NO:264, SEQ ID NO:297, SEQ ID NO:304, SEQ ID NO:310, or SEQ ID NO:312.

The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 8 amino acid positions from the sequence SEQ ID NO:298 (clone M39), that is, comprises a sequence which is at least 95% identical to

SEQ ID NO:298, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:53, SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:86, SEQ ID NO:89, SEQ ID NO:102, SEQ ID NO:106, SEQ ID NO:108, SEQ ID NO:118, SEQ ID NO:143, SEQ ID NO:150, SEQ ID NO:212, SEQ ID NO:227, SEQ ID NO:271, SEQ ID NO:292, or SEQ ID NO:298. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 6 amino acid positions from the sequence SEQ ID NO:298, that is, comprises a sequence which is at least 96% identical to SEQ ID NO:298, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:82, SEQ ID NO:86, SEQ ID NO:102, SEQ ID NO:106, SEQ ID NO:108, or SEQ ID NO:298. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 3 amino acid positions from the sequence SEQ ID NO:298, that is, comprises a sequence which is at least 98% identical to SEQ ID NO:298, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:102 or SEQ ID NO:298.

The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 8 amino acid positions from the sequence SEQ ID NO:303 (clone M17), that is, comprises a sequence which is at least 95% identical to SEQ ID NO:303, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:15, SEQ ID NO:20, SEQ ID NO:27, SEQ ID NO:74, SEQ ID NO:235, SEQ ID NO:256, or SEQ ID NO:303. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 6 amino acid positions from the sequence SEQ ID NO:303 , that is, comprises a sequence which is at least 96% identical to SEQ ID NO:303, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:15, SEQ ID NO:20, SEQ ID NO:27, SEQ ID NO:74, SEQ ID NO:256, or SEQ ID NO:303. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 3 amino acid positions from the sequence SEQ ID NO:303, that is, comprises a sequence which is at least 98% identical to SEQ ID NO:303, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:20, SEQ ID NO:256, or SEQ ID NO:303.

The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 8 amino acid positions from the sequence SEQ ID NO:306 (clone M18), that is, comprises a sequence which is at least 95% identical to SEQ ID NO:306, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:5, SEQ ID NO:10, SEQ ID NO:23, SEQ ID NO:31, SEQ ID NO:36, SEQ ID NO:47, SEQ ID NO:65, SEQ ID NO:71, SEQ ID NO:153, SEQ ID NO:159, SEQ ID NO:166, SEQ ID NO:200, SEQ ID NO:205, SEQ ID NO:230, SEQ ID NO:306, or SEQ ID NO:308. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 6 amino acid positions from the sequence SEQ ID NO:306, that is, comprises a sequence which is at least 96% identical to SEQ ID NO:306, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:5, SEQ ID NO:23, SEQ ID NO:31, SEQ ID NO:36, SEQ ID NO:47, SEQ ID NO:65, SEQ ID NO:153, SEQ ID NO:166, SEQ ID NO:200, SEQ ID NO:205, SEQ ID NO:230, SEQ ID NO:306, or SEQ ID NO:308. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 3 amino acid positions from the sequence SEQ ID NO:306, that is, comprises a sequence which is at least 98% identical to SEQ ID NO:306, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:5, SEQ ID NO:31, SEQ ID NO:47, SEQ ID NO:205, SEQ ID NO:230, SEQ ID NO:306, or SEQ ID NO:308.

The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 8 amino acid positions from the sequence SEQ ID NO:310 (clone M24), that is, comprises a sequence which is at least 95% identical to SEQ ID NO:310, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:12, SEQ ID NO:39, SEQ ID NO:46, SEQ ID NO:77, SEQ ID NO:216, SEQ ID NO:239, SEQ ID NO:241, SEQ ID NO:243, SEQ ID NO:250, SEQ ID NO:262, SEQ ID NO:264, SEQ ID NO:297, SEQ ID NO:304, SEQ ID NO:310, or SEQ ID NO:312. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 6 amino acid positions from the sequence SEQ ID NO:310, that is, comprises a sequence which is at least 96% identical to SEQ ID NO:310, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:39, SEQ ID

NO:46, SEQ ID NO:77, SEQ ID NO:216, SEQ ID NO:239, SEQ ID NO:241, SEQ ID NO:243, SEQ ID NO:250, SEQ ID NO:262, SEQ ID NO:264, SEQ ID NO:297, SEQ ID NO:304, SEQ ID NO:310, or SEQ ID NO:312. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 3 amino acid positions from the sequence SEQ ID NO:310, that is, comprises a sequence which is at least 98% identical to SEQ ID NO:310, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:39, SEQ ID NO:77, SEQ ID NO:216, SEQ ID NO:239, SEQ ID NO:241, SEQ ID NO:243, SEQ ID NO:250, SEQ ID NO:264, SEQ ID NO:297, SEQ ID NO:304, SEQ ID NO:310, or SEQ ID NO:312.

The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 8 amino acid positions from the sequence SEQ ID NO:312 (clone M01), that is, comprises a sequence which is at least 95% identical to SEQ ID NO:312, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:12, SEQ ID NO:39, SEQ ID NO:46, SEQ ID NO:77, SEQ ID NO:216, SEQ ID NO:232, SEQ ID NO:239, SEQ ID NO:241, SEQ ID NO:243, SEQ ID NO:250, SEQ ID NO:262, SEQ ID NO:264, SEQ ID NO:297, SEQ ID NO:304, SEQ ID NO:310, or SEQ ID NO:312. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 6 amino acid positions from the sequence SEQ ID NO:312, that is, comprises a sequence which is at least 96% identical to SEQ ID NO:312, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:39, SEQ ID NO:46, SEQ ID NO:77, SEQ ID NO:216, SEQ ID NO:239, SEQ ID NO:241, SEQ ID NO:243, SEQ ID NO:250, SEQ ID NO:262, SEQ ID NO:264, SEQ ID NO:297, SEQ ID NO:304, SEQ ID NO:310, or SEQ ID NO:312. The invention also includes an isolated or recombinant polypeptide which comprises a sequence which differs in 0 to 3 amino acid positions from the sequence SEQ ID NO:312, that is, comprises a sequence which is at least 98% identical to SEQ ID NO:312, and which exhibits an interferon-alpha activity; such as, for example, a polypeptide comprising the sequence SEQ ID NO:77, SEQ ID NO:216, SEQ ID NO:241, SEQ ID NO:243, SEQ ID NO:250, SEQ ID NO:264, SEQ ID NO:297, SEQ ID NO:304, SEQ ID NO:310, or SEQ ID NO:312.

Other modifications contemplated for polypeptides of the invention include those described below and in the section entitled "INTERFERON-ALPHA CONJUGATES".

Sequence Variations

As noted above, polypeptides of the present invention include polypeptides comprising sequences which differ from one of SEQ ID NO:1-SEQ ID NO:319 in 0 to 16 amino acid positions. Some such polypeptides exhibit an interferon-alpha activity.

For example, some polypeptides of the invention comprise a sequence having a length of about 151 amino acids, such as about 151, 152, 153, 154, 155 ,156, 157, 158, 159, 160, 161, 162, 163, 164, or 165 amino acids, corresponding to a deletion of between 1 and 15 amino acids relative to a parent polypeptide sequence (such as, for example, one of SEQ ID NOs:1-319). In some instances, between 1 and 11, e.g., between 1 and 10, such as between 1 and 7, e.g. between 1 and 5, such as between 1 and 3 amino acids are deleted from the C-terminus, i.e. the polypeptide is C-terminally truncated compared to the parent polypeptide sequence (such as, for example, one of SEQ ID NOs: 1-319) by 1-11 amino acid residues (e.g. by 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 amino acid residues), such as by 1-10, 1-7, e.g., by 1-5 or by 1-3 amino acid residues. Alternatively, or in addition, some such polypeptides are N-terminally truncated compared to the parent polypeptide sequence (such as, one of SEQ ID NOs: 1-319) by 1-4 amino acid residues (e.g. by 1, 2, 3, or 4 amino acid residues), e.g., 1-4, 1-3, 1-2 or 1 amino acid residue(s) are removed from the N-terminus. Some such polypeptides further comprise a methionine at the N-terminus. Some such polypeptides exhibit an interferon-alpha activity.

As another example, some polypeptides of the invention comprise a sequence containing between 1 and 16 amino acid substitutions relative to SEQ ID NO:1 (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, or 16 amino acid substitutions), such as 1-14 or 1-12 or 1-10 or 1-8 or 1-7 or 1-6 or 1-5 or 1-4 or 1-3 or 1-2 amino acid substitutions. One or more amino acid substitutions may be made in the polypeptide sequence according to, for example, a substitution group (such as, a conservative substitution group), such as one set forth below. Alternatively, or in addition, one or more additional amino acid substitutions may made in the polypeptide sequence which introduces or removes an amino acid residue comprising an attachment group for a non-polypeptide moiety. Examples include introduction or removal of one or more N-glycosylation site(s),

introduction or removal of one or more cysteine residue(s) or lysine residue(s) or histidine residue(s), and the like. Some such polypeptides exhibit an interferon-alpha activity.

As a non-limiting example, a polypeptide of the invention may have a sequence which differs from SEQ ID NO:1 in a total of up to 16 positions (which may be a combination of amino acid substitutions, deletions, and/or insertions, including those described above). In some instances, none, some, or all of the substitutions are substitutions according to a substitution group defined below.

Amino acid substitutions in accordance with the invention may include, but are not limited to, one or more conservative amino acid substitutions. Conservative substitution tables providing functionally similar amino acids are well known in the art. One example is provided in the table below (Table 1), which sets forth six exemplary groups that contain amino acids which may be considered "conservative substitutions" for one another.

Table 1
Conservative Substitution Groups

1	Alanine (A)	Glycine (G)	Serine (S)	Threonine (T)
2	Aspartic acid (D)	Glutamic acid (E)		
3	Asparagine (N)	Glutamine (Q)		
4	Arginine (R)	Lysine (K)	Histidine (H)	
5	Isoleucine (I)	Leucine (L)	Methionine (M)	Valine (V)
6	Phenylalanine (F)	Tyrosine (Y)	Tryptophan (W)	

Other substitution groups of amino acids can be envisioned. For example, amino acids can be grouped by similar function or chemical structure or composition (e.g., acidic, basic, aliphatic, aromatic, sulfur-containing). For example, an *Aliphatic* grouping may comprise: Glycine (G), Alanine (A), Valine (V), Leucine (L), Isoleucine (I). Other groups containing amino acids that are considered conservative substitutions for one another include: *Aromatic*: Phenylalanine (F), Tyrosine (Y), Tryptophan (W); *Sulfur-containing:* Methionine (M), Cysteine (C); *Basic*: Arginine (R), Lysine (K), Histidine (H); *Acidic*: Aspartic acid (D), Glutamic acid (E), Asparagine (N), Glutamine (Q). See also Creighton (1984) *Proteins*, W.H. Freeman and Company, for additional groupings of amino acids. Listing of a polypeptide sequence herein, in conjunction with the above

substitution groups, provides an express listing of all conservatively substituted polypeptide sequences.

Percent Sequence Identity

In one aspect, the invention provides isolated or recombinant polypeptides each comprising a sequence having at least 90% sequence identity (e.g., at least about 91%, at least about 92%, at least about 93%, at least about 94%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, or at least about 99% amino acid sequence identity) to any one of SEQ ID NOs:1-319. In some instances the polypeptide exhibits an interferon-alpha activity.

The degree to which a sequence (polypeptide or nucleic acid) is similar to another provides an indication of similar structural and functional properties for the two sequences. Accordingly, in the context of the present invention, sequences which have a similar sequence to any given exemplar sequence are a feature of the present invention. In particular, sequences that have percent sequence identities as defined below are a feature of the invention.

A variety of methods of determining sequence relationships can be used, including manual alignment and computer assisted sequence alignment and analysis. A variety of computer programs for performing sequence alignments are available, or an alignment can be prepared manually by one of skill, as described below.

As noted above, the sequences of the polypeptides and nucleic acids employed in the subject invention need not be identical, but can be substantially identical to the corresponding sequence of a polypeptide of the invention or nucleic acid of the invention. For example, polypeptides of the invention can be subject to various changes, such as one or more amino acid insertions, deletions, and/or substitutions, either conservative or non-conservative, including where, e.g., such changes might provide for certain advantages in their use, such as, in their therapeutic or prophylactic use or administration or diagnostic application. The nucleic acids of the invention can also be subject to various changes, such as one or more substitutions of one or more nucleic acids in one or more codons such that a particular codon encodes the same or a different amino acid, resulting in either a silent variation (as defined herein) or non-silent variation, or one or more deletions of one or more nucleic acids (or codons) in the sequence. The nucleic acids can also be modified to include one or more codons that provide for optimum expression in an

expression system (e.g., bacterial or mammalian), while, if desired, said one or more codons still encode the same amino acid(s). Such nucleic acid changes might provide for certain advantages in their therapeutic or prophylactic use or administration, or diagnostic application. The nucleic acids and polypeptides can be modified in a number of ways so long as they comprise a sequence substantially identical (as defined below) to a sequence in a respective nucleic acid or polypeptide of the invention.

The term "identical" or "identity," in the context of two or more nucleic acid or polypeptide sequences, refers to two or more sequences that are the same or have a specified percentage of amino acid residues or nucleotides that are the same, when compared and aligned for maximum similarity, as determined using the sequence comparison algorithm described below or by visual inspection.

The "percent sequence identity" ("% identity") of a subject sequence to a reference (i.e. query) sequence means that the subject sequence is identical (i.e., on an amino acid-by-amino acid basis for a polypeptide sequence, or a nucleotide-by-nucleotide basis for a polynucleotide sequence) by a specified percentage to the query sequence over a comparison length.

The percent sequence identity of a subject sequence to a query sequence is calculated as follows. First, the optimal alignment of the two sequences is determined using a sequence comparison algorithm with specific alignment parameters. This determination of the optimal alignment may be performed using a computer, or may be manually calculated, as described below. Then, the two optimally aligned sequences are compared over the comparison length, and the number of positions in the optimal alignment at which identical residues occur in both sequences are determined, which provides the number of matched positions. The number of matched positions is then divided by the total number of positions of the comparison length (which, unless otherwise specified, is the length of the query sequence), and then the result is multiplied by 100, to yield the percent sequence identity of the subject sequence to the query sequence.

With regard to polypeptide sequences, typically one sequence is regarded as a "query sequence" (for example, a polypeptide sequence of the invention) to which one or more other sequences, i.e., "subject sequence(s)" (for example, sequences present in a sequence database) are compared. The sequence comparison algorithm uses the designated alignment parameters to determine the optimal alignment between the query sequence

and the subject sequence(s). When comparing a query sequence against a sequence database, such as, e.g., GENBANK® (Genetic Sequence Data Bank; U.S. Department of Health and Human Services) or GENESEQ® (Thomson Derwent; also available as DGENE® on STN), usually only the query sequence and the alignment parameters are input into the computer; optimal alignments between the input query sequence and each subject sequence present in the database are returned, generally for up to a desired number of subject sequences.

Two polypeptide sequences are "optimally aligned" when they are aligned using defined parameters, i.e., a defined amino acid substitution matrix, gap existence penalty (also termed gap open penalty), and gap extension penalty, so as to arrive at the highest similarity score possible for that pair of sequences. The BLOSUM62 matrix (Henikoff and Henikoff (1992) Proc. Natl. Acad. Sci. USA 89(22):10915-10919) is often used as a default scoring substitution matrix in polypeptide sequence alignment algorithms (such as BLASTP, described below). The gap existence penalty is imposed for the introduction of a single amino acid gap in one of the aligned sequences, and the gap extension penalty is imposed for each residue position in the gap. Unless otherwise stated, alignment parameters employed herein are: BLOSUM62 scoring matrix, gap existence penalty = 11, and gap extension penalty = 1. The alignment score is defined by the amino acid positions of each sequence at which the alignment begins and ends (e.g. the alignment window), and optionally by the insertion of a gap or multiple gaps into one or both sequences, so as to arrive at the highest possible similarity score.

While optimal alignment between two or more sequences can be determined manually (as described below), the process is facilitated by the use of a computer-implemented alignment algorithm such as BLAST® (National Library of Medicine), e.g., BLASTP for polypeptide sequences and BLASTN for nucleic acid sequences, described in Altschul *et al.* (1997) Nucleic Acids Res. 25:3389-3402, and made available to the public through various sources, such as the National Center for Biotechnology Information (NCBI) Website. When using a computerized BLAST interface, if the option exists to use a "low complexity filter", this option should be turned off (i.e., no filter).

The optimal alignment between two polypeptide sequences can also be determined by a manual calculation of the BLASTP algorithm (i.e., without aid of a computer) using the same alignment parameters specified above (matrix = BLOSUM62, gap open penalty

= 11, and gap extension penalty = 1). To begin, the two sequences are initially aligned by visual inspection. An initial alignment score is then calculated as follows: for each individual position of the alignment (i.e., for each pair of aligned residues), a numerical value is assigned according to the BLOSUM62 matrix (Fig. 4). The sum of the values assigned to each pair of residues in the alignment is the initial alignment score. If the two sequences being aligned are highly similar, often this initial alignment provides the highest possible alignment score. The alignment with the highest possible alignment score is the optimal alignment based on the alignment parameters employed. Fig. 5A shows an example of the calculation of an alignment score for two sequences, a "query" sequence, identified herein as residues 29-50 of SEQ ID NO:1 (upper), and a "subject" sequence, identified herein as residues 30-52 of SEQ ID NO:312 (lower). The sequences were aligned by visual inspection, and the numerical value assigned by the BLOSUM62 matrix for each aligned pair of amino acids is shown beneath each position in the alignment (to aid in visualization, each identical pair of amino acids in the alignment is shown in boldface). In this example, this initial alignment provided the highest possible alignment score (the sum of the values shown beneath each aligned position); any other alignment of these two sequences, with or without gaps, would result in a lower alignment score.

In some instances, a higher alignment score might be obtained by introducing one or more gaps into the alignment. Whenever a gap is introduced into an alignment, a gap open penalty is assigned, and in addition a gap extension penalty is assessed for each residue position within that gap. Therefore, using the alignment parameters described above (including gap open penalty = 11 and gap extension penalty = 1), a gap of one residue in the alignment would correspond to a value of - (11+(1 x 1)) = -12 assigned to the gap; a gap of three residues would correspond to a value of - (11+(3 x 1)) = -14 assigned to the gap, and so on. This calculation is repeated for each new gap introduced into the alignment. Figs. 5B and 5C show an example which demonstrates how introduction of a gap into an alignment can result in a higher alignment score, despite the gap penalty. Fig. 5B shows an initial alignment of residues 29-50 of SEQ ID NO:312 (upper, query) and residues 30-50 of SEQ ID NO:321 (lower, subject) made by visual inspection, which results in an initial alignment score of 70. Fig. 5C shows the effect of the introduction of a one-residue gap in SEQ ID NO:321 on the alignment score; despite

the gap penalty of −12, the overall alignment score of the two sequences increases to 93. In this example, the alignment shown in Fig. 5C provides the highest possible alignment score, and is thus the optimal alignment of these two sequences; any other alignment of these two sequences (with or without gaps) would result in a lower alignment score.

It is to be understood that the examples of sequence alignment calculations described above, which use relatively short sequences, are provided for illustrative purposes only; in practice, the alignment parameters employed (BLOSUM62 matrix, gap open penalty = 11, and gap extension penalty = 1) are generally intended for polypeptide sequences 85 amino acids in length or longer. The NCBI website provides the following alignment parameters for sequences of other lengths (which are suitable for computer-aided as well as manual alignment calculation, using the same procedure as described above). For sequences of 50-85 amino acids in length, optimal parameters are BLOSUM80 matrix (Henikoff and Henikoff, *supra*), gap open penalty = 10, and gap extension penalty = 1. For sequences of 35-50 amino acids in length, optimal parameters are PAM70 matrix (Dayhoff, M.O., Schwartz, R.M. & Orcutt, B.C. (1978) "A model of evolutionary change in proteins." In Atlas of Protein Sequence and Structure, vol. 5, suppl. 3, M.O. Dayhoff (ed.), pp. 345-352, Natl. Biomed. Res. Found.,Washington, DC.), gap open penalty = 10, and gap extension penalty = 1. For sequences of less than 35 amino acids in length, optimal parameters are PAM30 matrix (Dayhoff, M.O., *supra*), gap open penalty = 9, and gap extension penalty = 1.

Once the sequences are optimally aligned, the percent identity of the subject sequence relative to the query sequence is calculated by counting the number of positions in the optimal alignment which contain identical residue pairs, divide that by the number of residues in the comparison length (which, unless otherwise specified, is the number of residues in the query sequence), and multiplying the resulting number by 100. Referring back to the examples shown in Figs. 5A-5C, in each example the sequence designated as the query (upper) sequence is 22 amino acids in length. In the alignment of Fig. 5A, 18 pairs of aligned amino acid residues (shown in boldface) are identical in the optimal alignment of the query sequence (upper) with the subject sequence (lower). Thus, this particular subject sequence has (18/22) x 100 = 81.8% identity to the entire length of the 22-residue query sequence; in other words, the subject sequence in the alignment of Fig. 5A has at least 81% amino acid sequence identity to the query sequence. In the alignment

shown in Fig. 5C, 18 pairs of amino acid residues (shown in boldface) in the optimal alignment are identical; thus this particular subject sequence has (18/22) x 100 = 81.8% identity to the entire length of the 22-residue query sequence; in other words, the subject sequence in the alignment of Fig. 5C has at least 81% amino acid sequence identity to the query sequence.

As applied to polypeptides, the term "substantial identity" (or "substantially identical") typically means that when two amino acid sequences (i.e. a query sequence and a subject sequence) are optimally aligned using the BLASTP algorithm (manually or via computer) using appropriate parameters described above, the subject sequence has at least about 60% , 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more percent amino acid sequence identity to the query sequence. In some instances, the substantial identity exists over a comparison length of at least about 100 amino acid residues, such as, at least about 110, 120, 125, 130, 135, 140, 145, 150, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, or 166 amino acid residues.

Similarly, as applied in the context of two nucleic acid sequences, the term substantial identity (or substantially identical) means that when two nucleic acid sequences (i.e. a query and a subject sequence) are optimally aligned using the BLASTN algorithm (manually or via computer) using appropriate parameters described below, the subject sequence has at least about 60%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more percent nucleic acid sequence identity to the query sequence. Parameters used for nucleic acid sequence alignments are: match reward 1, mismatch penalty -3, gap existence penalty 5, gap extension penalty 2 (substitution matrices are not used in the BLASTN algorithm). In some instances, the substantial identity exists over a comparison length of at least about 300 nucleotide residues, such as at least about 330, 360, 375, 390, 405, 420, 435, 450, 465, 480, 483, 486, 489, 492, 495, or 498 nucleotides.

Additional Aspects

Any polypeptide of the invention may be present as part of a larger polypeptide sequence, e.g. a fusion protein, such as occurs upon the addition of one or more domains or subsequences for stabilization or detection or purification of the polypeptide. A polypeptide purification subsequence may include, e.g., an epitope tag, a FLAG tag, a polyhistidine sequence, a GST fusion, or any other detection/purification subsequence or

"tag" known in the art. These additional domains or subsequences either have little or no effect on the activity of the polypeptide of the invention, or can be removed by post synthesis processing steps such as by treatment with a protease, inclusion of an intein, or the like.

The invention includes fusion proteins comprising a polypeptide of the invention, e.g., as described herein, fused to an Ig molecule, e.g., a human IgG Fc ("fragment crystallizable," or fragment complement binding) hinge, CH2 domain and CH3 domain, and nucleotide sequences encoding such fusion protein. Fc is the portion of the antibody responsible for binding to antibody receptors on cells and the C1q component of complement. These fusion proteins and their encoding nucleic acids are useful as prophylactic and/or therapeutic drugs or as diagnostic tools (see also, e.g., Challita-Eid, P. et al. (1998) J Immunol 160:3419-3426; Sturmhoefel, K. et al. (1999) Cancer Res 59:4964-4972). The invention also includes fusion proteins comprising a polypeptide of the invention, fused to an albumin molecule, such as human serum albumin (HSA), as described, for example, in U.S. Patent No. 5,876,969, and nucleotide sequences encoding the fusion protein. The Ig and albumin fusion proteins may exhibit increased polypeptide serum half-life and/or functional *in vivo* half-life, reduced polypeptide antigenicity, increased polypeptide storage stability, or increasing bioavailability, e.g. increased AUC_{sc}, and are thus may be useful as pprophylactic and/or therapeutic drugs.

Any polypeptide of the invention may also comprise one or more modified amino acid. The modified amino acid may be, e.g., a glycosylated amino acid, a PEGylated amino acid, a farnesylated amino acid, an acetylated amino acid, a biotinylated amino acid, an amino acid conjugated to a lipid moiety, or an amino acid conjugated to an organic derivatizing agent. The presence of modified amino acids may be advantageous in, for example, (a) increasing polypeptide serum half-life and/or functional *in vivo* half-life, (b) reducing polypeptide antigenicity, (c) increasing polypeptide storage stability, or (d) increasing bioavailability, e.g. increasing the AUC_{sc}. Amino acid(s) are modified, for example, co-translationally or post-translationally during recombinant production (e.g., N-linked glycosylation at N-X-S/T motifs during expression in mammalian cells) or modified by synthetic means. This aspect is described in more detail in the section herein entitled "INTERFERON-ALPHA CONJUGATES".

The invention also provides a composition comprising at least one polypeptide of the invention, and an excipient or carrier. The composition may be a composition comprising a pharmaceutically acceptable excipient or carrier. Exemplary compositions and excipients and carriers are described below.

Making Polypeptides

Recombinant methods for producing and isolating polypeptides of the invention are described herein. In addition to recombinant production, the polypeptides may be produced by direct peptide synthesis using solid-phase techniques (see, e.g., Stewart et al. (1969) Solid-Phase Peptide Synthesis, WH Freeman Co, San Francisco; Merrifield J. (1963) J Am Chem Soc 85:2149-2154). Peptide synthesis may be performed using manual techniques or by automation. Automated synthesis may be achieved, for example, using Applied Biosystems 431A Peptide Synthesizer (Perkin Elmer, Foster City, Calif.) in accordance with the instructions provided by the manufacturer. For example, subsequences may be chemically synthesized separately and combined using chemical methods to provide full-length polypeptides or fragments thereof. Alternatively, such sequences may be ordered from any number of companies which specialize in production of polypeptides. Most commonly, polypeptides of the invention may be produced by expressing coding nucleic acids and recovering polypeptides, e.g., as described below.

Methods for producing the polypeptides of the invention are also included. One such method comprises introducing into a population of cells any nucleic acid of the invention described herein, which is operatively linked to a regulatory sequence effective to produce the encoded polypeptide, culturing the cells in a culture medium to express the polypeptide, and isolating the polypeptide from the cells or from the culture medium. An amount of nucleic acid sufficient to facilitate uptake by the cells (transfection) and/or expression of the polypeptide is utilized. The nucleic acid is introduced into such cells by any delivery method described herein, including, e.g., injection, gene gun, passive uptake, etc. The nucleic acid may be part of a vector, such as a recombinant expression vector, including a DNA plasmid vector, or any vector described herein. The nucleic acid or vector comprising a nucleic acid of the invention may be prepared and formulated as described herein, above. Such a nucleic acid or expression vector may be introduced into a population of cells of a mammal *in vivo*, or selected cells of the mammal (e.g., tumor

cells) may be removed from the mammal and the nucleic acid expression vector introduced *ex vivo* into the population of such cells in an amount sufficient such that uptake and expression of the encoded polypeptide results. Or, a nucleic acid or vector comprising a nucleic acid of the invention is produced using cultured cells *in vitro*. In one aspect, the method of producing a polypeptide of the invention comprises introducing into a population of cells a recombinant expression vector comprising any nucleic acid of the invention described herein in an amount and formula such that uptake of the vector and expression of the encoded polypeptide will result; administering the expression vector into a mammal by any introduction/delivery format described herein; and isolating the polypeptide from the mammal or from a byproduct of the mammal.

Antibodies

In another aspect of the invention, a polypeptide of the invention (or an antigenic fragment thereof) is used to produce antibodies which have, e.g., diagnostic, therapeutic, or prophylactic uses, e.g., related to the activity, distribution, and expression of polypeptides and fragments thereof. Antibodies to polypeptides of the invention may be generated by methods well known in the art. Such antibodies may include, but are not limited to, polyclonal, monoclonal, chimeric, humanized, single chain, Fab fragments and fragments produced by a Fab expression library. Antibodies, e.g., those that block receptor binding, are especially preferred for therapeutic and/or prophylactic use.

Polypeptides for antibody induction do not require biological activity; however, the polypeptides or peptides should be antigenic. Peptides used to induce specific antibodies may have an amino acid sequence consisting of at least about 10 amino acids, preferably at least about 15 or 20 amino acids or at least about 25 or 30 amino acids. Short stretches of a polypeptide may be fused with another protein, such as keyhole limpet hemocyanin, and antibody produced against the chimeric molecule.

Methods of producing polyclonal and monoclonal antibodies are known to those of skill in the art, and many antibodies are available. See, e.g., Current Protocols in Immunology, John Colligan *et al.*, eds., Vols. I-IV (John Wiley & Sons, Inc., NY, 1991 and 2001 Supplement); and Harlow and Lane (1989) Antibodies: A Laboratory Manual Cold Spring Harbor Press, NY; Stites et al. (eds.) Basic and Clinical Immunology (4th ed.) Lange Medical Publications, Los Altos, CA, and references cited therein; and Goding (1986) Monoclonal Antibodies: Principles and Practice (2d ed.) Academic Press, New

York, NY; and Kohler and Milstein (1975) Nature 256:495-497. Other suitable techniques for antibody preparation include selection of libraries of recombinant antibodies in phage or similar vectors. *See*, Huse et al. (1989) Science 246:1275-1281; and Ward et al. (1989) Nature 341:544-546. Specific monoclonal and polyclonal antibodies and antisera will usually bind with a K_D of at least about 0.1 μM, preferably at least about 0.01 μM or better, and most typically and preferably, 0.001 μM or better.

Detailed methods for preparation of chimeric (humanized) antibodies can be found in U.S. Patent 5,482,856. Additional details on humanization and other antibody production and engineering techniques can be found in Borrebaeck (ed.) (1995) Antibody Engineering, 2nd Edition Freeman and Company, NY (Borrebaeck); McCafferty et al. (1996) Antibody Engineering, A Practical Approach IRL at Oxford Press, Oxford, England (McCafferty), and Paul (1995) Antibody Engineering Protocols Humana Press, Towata, NJ (Paul).

In one aspect, this invention provides for fully humanized antibodies against the polypeptides of the invention or fragments thereof. Humanized antibodies are especially desirable in applications where the antibodies are used as therapeutics and/or prophylactics *in vivo* in human patients. Human antibodies consist of characteristically human immunoglobulin sequences. The human antibodies of this invention can be produced in using a wide variety of methods (see, e.g., Larrick et al., U.S. Pat. No. 5,001,065, and Borrebaeck McCafferty and Paul, *supra*, for a review). In one aspect, the human antibodies of the present invention are produced initially in trioma cells. Genes encoding the antibodies are then cloned and expressed in other cells, such as nonhuman mammalian cells. The general approach for producing human antibodies by trioma technology is described by Ostberg et al. (1983), Hybridoma 2:361-367, Ostberg, U.S. Pat. No. 4,634,664, and Engelman et al., U.S. Pat. No. 4,634,666. The antibody-producing cell lines obtained by this method are called triomas because they are descended from three cells – two human and one mouse. Triomas have been found to produce antibody more stably than ordinary hybridomas made from human cells.

Other uses contemplated for polypeptides of the invention are provided throughout the specification.

INTERFERON-ALPHA CONJUGATES

In another aspect, the invention relates to a conjugate comprising a polypeptide exhibiting an interferon-alpha activity which comprises an amino acid sequence of any one of SEQ ID NOs:1-319, and at least one non-polypeptide moiety attached to the polypeptide, such as e.g., 1-6, 1-5, 1-4, 1-3, e.g. 1 or 2 non-polypeptide moieties attached to the polypeptide. It will be understood that the conjugate also exhibits an interferon-alpha activity (such as, antiviral activity, T_H1 differentiation activity, and/or antiproliferative activity). Some such conjugates further comprise one or more additional amino acid(s), such as a methionine added to the N-terminus of the polypeptide.

In another aspect the conjugate comprises a polypeptide exhibiting an interferon-alpha activity which comprises an amino acid sequence which differs in 0 to 16 amino acid positions from one of SEQ ID NO:1-SEQ ID NO:319, and at least one non-polypeptide moiety attached to the polypeptide, such as e.g., 1-6, 1-5, 1-4, 1-3, e.g. 1 or 2 non-polypeptide moieties attached to the polypeptide. In some instances, the amino acid sequence comprises one or more substitutions which introduces or removes an attachment group for the non-polypeptide moiety (e.g., by substitution of an amino acid residue for a different residue which comprises an attachment group for the non-polypeptide moiety, or by insertion of an additional amino acid residue which comprises an attachment group for the non-polypeptide moiety). It will be understood that the conjugate also exhibits an interferon-alpha activity (such as, antiviral activity, T_H1 differentiation activity, and/or antiproliferative activity). Some such conjugates further comprise one or more additional amino acid(s), such as a methionine added to the N-terminus of the polypeptide.

The term "conjugate" (or interchangeably "polypeptide conjugate" or "conjugated polypeptide") is intended to indicate a heterogeneous (in the sense of composite) molecule formed by the covalent attachment of one or more polypeptides of the invention to one or more non-polypeptide moieties. The term "covalent attachment" means that the polypeptide and the non-polypeptide moiety are either directly covalently joined to one another, or else are indirectly covalently joined to one another through an intervening moiety or moieties, such as a bridge, spacer, or linkage moiety or moieties. Preferably, a conjugated polypeptide is soluble at relevant concentrations and conditions, i.e. soluble in physiological fluids such as blood. Examples of conjugated polypeptides of the invention

include glycosylated and/or PEGylated polypeptides. The term "non-conjugated polypeptide" may be used to refer to the polypeptide part of the conjugated polypeptide.

The term "non-polypeptide moiety" is intended to mean a molecule that is capable of conjugating to an attachment group of the polypeptide. Preferred examples of non-polypeptide moieties include polymer molecules, sugar moieties, lipophilic compounds, or organic derivatizing agents, in particular polymer molecules or sugar moieties. It will be understood that the non-polypeptide moiety is linked to the polypeptide through an attachment group of the polypeptide. Except where the number of non-polypeptide moieties, such as polymer molecule(s), attached to the polypeptide is expressly indicated, every reference to "a non-polypeptide moiety" attached to the polypeptide or otherwise used in the present invention shall be a reference to one or more non-polypeptide moieties attached to the polypeptide.

The term "polymer molecule" is defined as a molecule formed by covalent linkage of two or more monomers, wherein none of the monomers is an amino acid residue. The term "polymer" may be used interchangeably with the term "polymer molecule".

The term "sugar moiety" is intended to indicate a carbohydrate molecule attached by *in vivo* or *in vitro* glycosylation, such as N- or O-glycosylation.

An "N-glycosylation site" has the sequence N-X-S/T/C, wherein X is any amino acid residue except proline, N is asparagine and S/T/C is either serine, threonine or cysteine, preferably serine or threonine, and most preferably threonine.

An "O-glycosylation site" comprises the OH-group of a serine or threonine residue.

The term "attachment group" is intended to indicate an amino acid residue group capable of coupling to the relevant non-polypeptide moiety such as a polymer molecule or a sugar moiety. Non-limiting examples of useful attachment groups and some corresponding non-polypeptide moieties are provided in Table 2 below.

Table 2

Useful attachment groups and examples of corresponding non-polypeptide moieties

Attachment group	Amino acid	Examples of non-polypeptide moieties	Examples of conjugation method / activated PEG	Reference
$-NH_2$	N-terminus, Lys	Polymer, e.g. PEG	mPEG-SPA mPEG2-NHS mPEG2-butryALD	Nektar Inc. 2003 Catalog
-COOH	C-terminus, Asp, Glu	Polymer, e.g. PEG Sugar moiety	mPEG-Hz *In vitro* coupling	Nektar Inc. 2003 Catalog
-SH	Cys	Polymer, e.g. PEG, Sugar moiety	mPEG-VS mPEG2-MAL *In vitro* coupling	Nektar Inc. 2003 Catalog; Delgado et al, Critical Reviews in Therapeutic Drug Carrier Systems 9(3,4):249-304 (1992)
-OH	Ser, Thr, OH-	Sugar moiety	*In vivo* O-linked glycosylation	
$-CONH_2$	Asn as part of an N-glycosylation site	Sugar moiety	*In vivo* N-glycosylation	
Aromatic residue	Phe, Tyr, Trp	Sugar moiety	*In vitro* coupling	
$-CONH_2$	Gln	Sugar moiety	*In vitro* coupling	Yan and Wold, Biochemistry, 1984, Jul 31; 23(16): 3759-65
Aldehyde Ketone	Oxidized carbohydrate	Polymer, e.g. PEG, PEG-hydrazide	PEGylation	Andresz et al., 1978, Makromol. Chem. 179:301; WO 92/16555, WO 00/23114
Guanidino	Arg	Sugar moiety	*In vitro* coupling	Lundblad and Noyes, Chemical Reagents for Protein Modification, CRC Press Inc. Boca Raton, Fl

Attachment group	Amino acid	Examples of non-polypeptide moieties	Examples of conjugation method / activated PEG	Reference
Imidazole ring	His	Sugar moiety	*In vitro* coupling	As for guanidine

For *in vivo* N-glycosylation, the term "attachment group" is used in an unconventional way to indicate the amino acid residues constituting an N-glycosylation site (with the sequence N-X-S/T/C, wherein X is any amino acid residue except proline, N is asparagine and S/T/C is either serine, threonine or cysteine, preferably serine or threonine, and most preferably threonine). Although the asparagine residue of the N-glycosylation site is the one to which the sugar moiety is attached during glycosylation, such attachment cannot be achieved unless the other amino acid residues of the N-glycosylation site is present. Accordingly, when the non-polypeptide moiety is a sugar moiety and the conjugation is to be achieved by N-glycosylation, the term "amino acid residue comprising an attachment group for the non-polypeptide moiety" as used in connection with alterations of the amino acid sequence of the polypeptide of the invention is to be understood as one, two or all of the amino acid residues constituting an N-glycosylation site is/are to be altered in such a manner that either a functional N-glycosylation site is introduced into the amino acid sequence, removed from said sequence or a functional N-glycosylation site is retained in the amino acid sequence (e.g. by substituting a serine residue, which already constitutes part of an N-glycosylation site, with a threonine residue and *vice versa*).

The term "introduce" (i.e., an "introduced" amino acid residue, "introduction" of an amino acid residue) is primarily intended to mean substitution of an existing amino acid residue for another amino acid residue, but may also mean insertion of an additional amino acid residue.

The term "remove" (i.e., a "removed" amino acid residue, "removal" of an amino acid residue) is primarily intended to mean substitution of the amino acid residue to be removed for another amino acid residue, but may also mean deletion (without substitution) of the amino acid residue to be removed.

The term "amino acid residue comprising an attachment group for the non-polypeptide moiety" is intended to indicate that the amino acid residue is one to which the

non-polypeptide moiety binds (in the case of an introduced amino acid residue) or would have bound (in the case of a removed amino acid residue).

The term "functional *in vivo* half-life" is used in its normal meaning, i.e. the time at which 50% of the biological activity of the polypeptide is still present in the body/target organ, or the time at which the activity of the polypeptide is 50% of the initial value. The functional *in vivo* half-life may be determined in an experimental animal, such as rat, mice, rabbit, dog or monkey. Preferably, the functional *in vivo* half-life is determined in a non-human primate, such as a monkey. Furthermore, the functional *in vivo* half-life may be determined for a sample that has been administered intravenously or subcutaneously.

As an alternative to determining functional *in vivo* half-life, "serum half-life" may be determined, i.e. the time at which 50% of the polypeptide circulates in the plasma or bloodstream prior to being cleared. Determination of serum half-life is often more simple than determining the functional *in vivo* half-life and the magnitude of serum half-life is usually a good indication of the magnitude of functional *in vivo* half-life. Alternatively terms to serum half-life include "plasma half-life", "circulating half-life", "serum clearance", "plasma clearance" and "clearance half-life". The serum half-life may be determined as described above in connection with determination of functional *in vivo* half-life.

The term "serum" is used in its normal meaning, i.e. as blood plasma without fibrinogen and other clotting factors.

The term "increased" as used about the functional *in vivo* half-life or serum half-life is used to indicate that the relevant half-life of the conjugate of the invention is statistically significantly increased relative to that of a reference molecule, such as a wild-type interferon-alpha, e.g., a human interferon-alpha, such as one of SEQ ID NO:320-SEQ ID NO:332 (or other huIFN-alpha sequences as described herein and/or in Allen G. and Diaz M.O. (1996), *supra)*, or the corresponding non-conjugated polypeptide. Thus, interesting conjugates of the invention include those which have an increased functional *in vivo* half-life or an increased serum half-life as compared to a reference molecule mentioned above.

The term "AUC_{sc}" or "Area Under the Curve when administered subcutaneously" is used in its normal meaning, i.e. as the area under the interferon-alpha-activity-in-serum vs. time curve, where the conjugated molecule has been administered subcutaneously to

an experimental animal. Once the experimental interferon-alpha activity time points have been determined, the AUC_{sc} may conveniently be calculated by a computer program, such as GraphPad Prism 3.01.

The term "increased" as used about the AUC_{sc} is used to indicate that the Area Under the Curve for a conjugate of the invention, when administered subcutaneously, is statistically significantly increased relative to that of a reference molecule, such as wild-type interferon-alpha, e.g., a human interferon-alpha, such as one of SEQ ID NO:320-SEQ ID NO:332 (or other huIFN-alpha sequences as described herein and/or in Allen G. and Diaz M.O. (1996), *supra)*, or the corresponding non-conjugated polypeptide, when determined under comparable conditions. Evidently, the same amount of interferon-alpha activity should be administered for the conjugate of the invention and the reference molecule. Consequently, in order to make direct comparisons between different interferon-alpha molecules, the AUC_{sc} values should typically be normalized, i.e. be expressed as AUC_{sc}/dose administered.

The term "$T_{max,sc}$" is used about the time point in the interferon-alpha-activity-in-serum vs. time curve where the highest interferon-alpha activity in serum is observed.

It will be understood that while the examples and modifications to the parent polypeptide are generally provided herein in regards to the sequence SEQ ID NO:1, the disclosed modifications may also be made in equivalent amino acid positions of any of the other polypeptides of the invention (including SEQ ID NO:2-SEQ ID NO:319 and variants thereof) described above.

By removing and/or introducing amino acid residues comprising an attachment group for the non-polypeptide moiety it is possible to specifically adapt the polypeptide so as to make the molecule more susceptible to conjugation to the non-polypeptide moiety of choice, to optimize the conjugation pattern (e.g. to ensure an optimal distribution of non-polypeptide moieties on the surface of the interferon-alpha molecule and thereby, e.g., effectively shield epitopes and other surface parts of the polypeptide without significantly impairing the function thereof). For instance, by introduction of attachment groups, the interferon-alpha polypeptide is altered in the content of the specific amino acid residues to which the relevant non-polypeptide moiety binds, whereby a more efficient, specific and/or extensive conjugation is achieved. By removal of one or more attachment groups it is possible to avoid conjugation to the non-

polypeptide moiety in parts of the polypeptide in which such conjugation is disadvantageous, e.g. to an amino acid residue located at or near a functional site of the polypeptide (since conjugation at such a site may result in inactivation or reduced interferon- alpha activity of the resulting conjugate due to impaired receptor recognition). Further, it may be advantageous to remove an attachment group located close to another attachment group.

It will be understood that the amino acid residue comprising an attachment group for a non-polypeptide moiety, whether it be removed or introduced, is selected on the basis of the nature of the non-polypeptide moiety and, in some instances, on the basis of the conjugation method to be used. For instance, when the non-polypeptide moiety is a polymer molecule, such as a polyethylene glycol or polyalkylene oxide derived molecule, amino acid residues capable of functioning as an attachment group may be selected from the group consisting of cysteine, lysine (and/or the N-terminal amino group of the polypeptide), aspartic acid, glutamic acid, histidine and arginine. When the non-polypeptide moiety is a sugar moiety, the attachment group is an *in vivo* or *in vitro* N- or O-glycosylation site, preferably an N-glycosylation site.

In some instances, when an attachment group for a non-polypeptide moiety is to be introduced into or removed from the interferon-alpha polypeptide, the position of the interferon-alpha polypeptide to be modified may be conveniently selected as follows:

The position to be modified may be located at the surface of the interferon-alpha polypeptide, such as a position occupied by an amino acid residue which has more than 25% of its side chain exposed to the solvent, such as more than 50% of its side chain exposed to the solvent. Such positions have been identified on the basis of an analysis of a 3D structure of the human interferon-alpha 2a molecule as described in the "Materials and Methods" section herein.

In order to determine an optimal distribution of attachment groups, the distance between amino acid residues located at the surface of the interferon-alpha molecule was calculated on the basis of a 3D structure of an interferon-alpha polypeptide. More specifically, the distance between the CB's of the amino acid residues comprising such attachment groups, or the distance between the functional group (NZ for lysine, CG for aspartic acid, CD for glutamic acid, SG for cysteine) of one and the CB of another amino acid residue comprising an attachment group were determined. In case of glycine, CA

was used instead of CB. In the interferon-α polypeptide part of a conjugate of the invention, any of said distances may be more than 8 Å, such as more than 10 Å in order to avoid or reduce heterogeneous conjugation and to provide a uniform distribution of attachment groups, e.g. with the aim of epitope shielding.

Furthermore, in the interferon-alpha polypeptide part of a conjugate of the invention, in some instances attachment groups located at or near the receptor binding sites of interferon-alpha are removed, such as by substitution of the amino acid residue comprising such group. In some instances, amino acid residues comprising an attachment group for a non-polypeptide moiety, such as cysteine or lysine, are often not introduced at or near the receptor binding site of the interferon alpha molecule.

Another approach for modifying an interferon-alpha polypeptide is to shield and thereby modify or destroy or otherwise inactivate an epitope present in the parent interferon-alpha, by conjugation to a non-polypeptide moiety. Epitopes of interferon-alpha polypeptides may be identified by use of methods known in the art, also known as epitope mapping, see e.g. Romagnoli et al., *J. Biol Chem.*, 1999, 380(5):553-9, DeLisser HM, *Methods Mol Biol*, 1999, 96:11-20, Van de Water et al., *Clin Immunol Immunopathol*, 1997, 85(3):229-35, Saint-Remy JM, *Toxicology*, 1997, 119(1):77-81, and Lane DP and Stephen CW, *Curr Opin Immunol*, 1993, 5(2):268-71. One method is to establish a phage display library expressing random oligopeptides of, e.g., 9 amino acid residues. IgG1 antibodies from specific antisera towards human interferon-alpha are purified by immunoprecipitation and the reactive phages are identified by immunoblotting. By sequencing the DNA of the purified reactive phages, the sequence of the oligopeptide can be determined followed by localization of the sequence on the 3D-structure of the interferon-alpha. Alternatively, epitopes can be identified according to the method described in US Patent 5,041,376. The thereby identified region on the structure constitutes an epitope that then can be selected as a target region for introduction of an attachment group for the non-polypeptide moiety. Preferably, at least one epitope, such as two, three or four epitopes of interferon-alpha are shielded by a non-polypeptide moiety according to the present invention. Accordingly, in one aspect, the conjugate of the invention has at least one shielded epitope as compared to a wild type human interferon-alpha, including any commercially available interferon- alpha. This may be done by introduction of an attachment group for a non-polypeptide moiety into a position located

in the vicinity of (i.e. within 4 amino acid residues in the primary sequence or within about 10 Å in the tertiary sequence) of a given epitope. The 10 Å distance is measured between CB's (CA's in case of glycine). Such specific introductions are described in the following sections.

In case of removal of an attachment group, the relevant amino acid residue comprising such group and occupying a position as defined above may be substituted with a different amino acid residue that does not comprise an attachment group for the non-polypeptide moiety in question, or may be deleted. Removal of an N-glycosylation group, may also be accomplished by insertion or removal of an amino acid reside within the motif N-X-S/T/C.

In case of introduction of an attachment group, an amino acid residue comprising such group is introduced into the position, such as by substitution of the amino acid residue occupying such position.

The exact number of attachment groups available for conjugation and present in the interferon-alpha polypeptide is dependent on the effect desired to be achieved by conjugation. The effect to be obtained is, e.g., dependent on the nature and degree of conjugation (e.g. the identity of the non-polypeptide moiety, the number of non-polypeptide moieties desirable or possible to conjugate to the polypeptide, where they should be conjugated or where conjugation should be avoided, etc.). For instance, if reduced immunogenicity is desired, the number (and location of) attachment groups should be sufficient to shield most or all epitopes. This is normally obtained when a greater proportion of the interferon-alpha polypeptide is shielded. Effective shielding of epitopes is normally achieved when the total number of attachment groups available for conjugation is in the range of 1-6 attachment groups, e.g., 1-5, such as in the range of 1-3, such as 1, 2, or 3 attachment groups.

Functional *in vivo* half-life is *i.a.* dependent on the molecular weight of the conjugate, and the number of attachment groups needed for providing increased half-life thus depends on the molecular weight of the non-polypeptide moiety in question. Some such conjugates comprise 1-6, e.g., 1-5, such as 1-3, e.g. 1, 2, or 3 non-polypeptide moieties each having a MW of about 2-40 kDa, such as about 2 kDa, about 5 kDa, about 12 kDa, about 15 kDa, about 20 kDa, about 30 kDa, or about 40 kDa.

In the conjugate of the invention, some, most, or substantially all conjugatable attachment groups are occupied by the relevant non-polypeptide moiety.

The conjugate of the invention may exhibit one or more of the following improved properties:

For example, the conjugate may exhibit a reduced immunogenicity as compared to the corresponding non-conjugated polypeptide, e.g. a reduction of at least 10%, such as a reduction of at least of 25%, such as a reduction of at least of 50%, e.g. a reduction of at least 75% compared to the non-conjugated polypeptide.

In another aspect the conjugate may exhibit a reduced reaction or no reaction with neutralizing antibodies from patients treated with a human interferon-alpha (such as any of the polypeptides defined herein as SEQ ID NO:320-SEQ ID NO:332, or any other huIFN-alpha described herein and/or in Allen G. and Diaz M.O. (1996), *supra*) or as compared to the corresponding non-conjugated polypeptide, e.g. a reduction of neutralisation of at least 10%, such as at least of 25%, such as of at least 50%, e.g., at least 75%.

In another aspect of the invention the conjugate may exhibit an increased functional *in vivo* half-life and/or increased serum half-life as compared to a reference molecule, such as a human interferon-alpha (e.g. any of the polypeptides defined herein as SEQ ID NO:320-332 or any other huIFN-alpha described herein and/or in Allen G. and Diaz M.O. (1996), *supra*) or a conjugated reference interferon-alpha (e.g., a conjugated human IFN-alpha 2a or a connjugated human IFN-alpha 2b), or as compared to the corresponding non-conjugated polypeptide. Particular preferred conjugates are such conjugates where the ratio between the functional *in vivo* half-life (or serum half-life) of said conjugate and the functional *in vivo* half-life (or serum half-life) of said reference molecule is at least 1.25, such as at least 1.50, such as at least 1.75, such as at least 2, such as at least 3, such as at least 4, such as at least 5, such as at least 6, such as at least 7, such as at least 8. As mentioned above, the half-life is conveniently determined in an experimental animal, such as rat or monkey, and may be based on intravenously or subcutaneously administration.

In a further aspect the conjugate may exhibit an increased bioavailability as compared to a reference molecule such as a human interferon-alpha (e.g. any of the polypeptides defined herein as SEQ ID NO:320-332, or any other huIFN-alpha described

herein and/or in Allen G. and Diaz M.O. (1996), *supra*) or a conjugated reference interferon-alpha (e.g., a conjugated human IFN-alpha 2a or a connjugated human IFN-alpha 2b), or the corresponding non-conjugated polypeptide. For example, the conjugate may exhibit an increased AUC_{sc} as compared to a reference molecule. Thus, exemplary conjugates are such conjugates where the ratio between the AUC_{sc} of said conjugate and the AUC_{sc} of said reference molecule is at least 1.25, such as at least 1.5, such as at least 2, such as at least 3, such as at least 4, such as at least 5 or at least 6, such as at least 7, such as at least 8, such as at least 9 or at least 10, such as at least 12, such as at least 14, e.g. at least 16, at least 18 or at least 20 when administered subcutaneously, in particular when administered subcutaneously in an experimental animal such as rat or monkey. Analogously, some conjugates of the invention are such conjugates wherein the ratio between T_{max} for said conjugate and T_{max} for said reference molecule, such as a human interferon-alpha or conjugate thereof or the corresponding non-conjugated polypeptide, is at least 1.2, such as at least 1.4, e.g. at least 1.6, such as at least 1.8, such as at least 2, e.g. at least 2.5, such as at least 3, such as at least 4, e.g. at least 5, such as at least 6, such as at least 7, e.g. at least 8, such as at least 9, such as at least 10, when administered subcutaneously, in particular when administered subcutaneously in an experimental animal such as rat or monkey.

In some instances, the magnitude of the antiviral activity of a conjugate of the invention may be reduced (e.g. by at least about 75%, at least about 50%, at least about 25%, at least about 10%) or increased (e.g. by at least about 10 %) or is about equal (e.g. within about +/- 10% or about +/- 5%) to that of a human interferon-alpha (e.g. any of the polypeptides identified herein as SEQ ID NO:320-332, or any other huIFN-alpha described herein and/or in Allen G. and Diaz M.O. (1996), *supra*) or to that of the corresponding non-conjugated polypeptide. In some instances the ratio of antiviral activity to antiproliferative activity of a conjugate of the invention may vary, and thus be higher, lower or about equal to that of a human interferon-alpha or to that of the corresponding non-conjugated polypeptide.

Conjugate of the invention where the non-polypeptide moiety binds to a lysine residue or the N-terminal amine

In one aspect, the invention relates to a conjugate exhibiting an interferon-alpha activity and comprising at least one non-polypeptide moiety conjugated to at least one

lysine residue and/or to the N-terminal amino group of an interferon-alpha polypeptide comprising a sequence selected from SEQ ID NOs:1-319.

In another aspect, the invention relates to a conjugate exhibiting an interferon-alpha activity and comprising at least one non-polypeptide moiety conjugated to at least one lysine residue, or to the N-terminal amino group, of an interferon-alpha polypeptide comprising a sequence which (a) differs in 1 to 16 amino acid positions (such as in 1-15 amino acid positions, in 1-14 amino acid positions, in 1-13 amino acid positions, in 1-12 amino acid positions, 1-11 amino acid positions, in 1-10 amino acid positions, in 1-9 amino acid positions, in 1-8 amino acid positions, in 1-7 amino acid positions, in 1-6 amino acid positions, in 1-5 amino acid positions, in 1-4 amino acid positions, in 1-3 amino acid positions, or in 1-2 amino acid positions) from one of SEQ ID NO:1-SEQ ID NO:319. Some conjugates according to this aspect comprise at least one removed lysine residue and/or at least one removed histidine residue, and/or at least one introduced lysine residue.

Non-polypeptide moieties contemplated for this aspect of the invention include polymer molecules, such as any of the molecules mentioned in the section entitled "Conjugation to a polymer molecule", such as PEG or mPEG. The conjugation between the lysine-containing polypeptide and the polymer molecule may be achieved in any suitable manner, e.g. as described in the section entitled "Conjugation to a polymer molecule", e.g. in using a one step method or in the stepwise manner referred to in said section. An exemplary method for PEGylating the interferon-alpha polypeptide is to covalently attach PEG to lysine residues using lysine-reactive PEGs. A number of highly specific, lysine-reactive PEGs (such as for example, succinimidyl propionate (SPA), succinimidyl butanoate (SBA), N-hydroxylsuccinimide (NHS), and aldehyde (e.g., ButyrALD)) and different size linear or branched PEGs (e.g., 2-40 kDa, such as 2 kDa, 5 kDa, 12 kDa, 15 kDa, 20 kDa, 30 kDa, or 40 kDa,) are commercially available, e.g. from Nektar Therapeutics Inc., Huntsville, AL, USA, or SunBio, Anyang City, South Korea.

Conjugate of the invention where the non-polypeptide moiety binds to a cysteine residue

In one aspect, the invention relates to a conjugate exhibiting an interferon-alpha activity and comprising at least one non-polypeptide moiety conjugated to at least one cysteine residue of an interferon-alpha polypeptide comprising a sequence which (a)

differs in 1 to 16 amino acid positions (such as in 1-15 amino acid positions, in 1-14 amino acid positions, in 1-13 amino acid positions, in 1-12 amino acid positions, 1-11 amino acid positions, in 1-10 amino acid positions, in 1-9 amino acid positions, in 1-8 amino acid positions, in 1-7 amino acid positions, in 1-6 amino acid positions, in 1-5 amino acid positions, in 1-4 amino acid positions, in 1-3 amino acid positions, or in 1-2 amino acid positions) from one of SEQ ID NO:1-319. Some conjugates according to this aspect comprise at least one introduced cysteine residue.

In some instances, only a single cysteine residue is introduced in order to avoid formation of disulfide bridges between two or more introduced cysteine residues.

In interferon alphas, disulfide bonds are formed between cysteines at positions 1/99 and 29/139. The disulfide bond 29/139 is essential for biological activity, while the1/99 bond can be reduced without significantly affecting biological activity (Beilharz M.W. *et al.* (1986) J. Interferon Res. 6(6):677-685). Thus, in another aspect of the invention one of C1 or C99 is removed, preferably by substitution, e.g. C1S or C99S, thereby leaving the other cysteine residue available for conjugation to a non-polypeptide moiety.

Non-polypeptide moieties contemplated in this aspect of the invention include polymer molecules, such as any of the molecules mentioned in the section entitled "Conjugation to a polymer molecule", such as PEG or mPEG. The conjugation between the cysteine-containing polypeptide and the polymer molecule may be achieved in any suitable manner, e.g. as described in the section entitled "Conjugation to a polymer molecule", e.g. in using a one step method or in the stepwise manner referred to in said section. An exemplary method for PEGylating the interferon-alpha polypeptide is to covalently attach PEG to cysteine residues using cysteine-reactive PEGs. A number of highly specific, cysteine-reactive PEGs with different groups (e.g. orthopyridyl-disulfide (OPSS), maleimide (MAL) and vinylsulfone (VS)) and different size linear or branched PEGs (e.g., 2-40 kDa, such as 2 kDa, 5 kDa, 12 kDa, 15 kDa, 20 kDa, 30 kDa, or 40 kDa) are commercially available, e.g. from Nektar Therapeutics Inc., Huntsville, AL, USA, or SunBio, Anyang City, South Korea.

Non-polypeptide moiety of the conjugate of the invention

As indicated above, the non-polypeptide moiety of the conjugate of the invention is generally selected from the group consisting of a polymer molecule, a lipophilic

compound, a sugar moiety (e.g., by way of *in vivo* N-glycosylation) and an organic derivatizing agent. All of these agents may confer desirable properties to the polypeptide part of the conjugate, such as reduced immunogenicity, increased functional *in vivo* half-life, increased serum half-life, increased bioavailability and/or increased AUC_{sc}. The polypeptide part of the conjugate is often conjugated to only one type of non-polypeptide moiety, but may also be conjugated to two or more different types of non-polypeptide moieties, e.g. to a polymer molecule and a sugar moiety, etc. The conjugation to two or more different non-polypeptide moieties may be done simultaneously or sequentially. The choice of non-polypeptide moiety/moieties, depends especially on the effect desired to be achieved by the conjugation. For instance, sugar moieties have been found particularly useful for reducing immunogenicity, whereas polymer molecules such as PEG are of particular use for increasing functional *in vivo* half-life and/or serum half-life. Using a combination of a polymer molecule and a sugar moiety may enhance the reduction in immunogenicity and the increase in functional *in vivo* or serum half-life.

In the following sections "Conjugation to a lipophilic compound", "Conjugation to a polymer molecule", "Conjugation to a sugar moiety" and "Conjugation to an organic derivatizing agent" conjugation to specific types of non-polypeptide moieties is described.

Conjugation to a lipophilic compound

For conjugation to a lipophilic compound the following polypeptide groups may function as attachment groups: the N-terminus or C-terminus of the polypeptide, the hydroxy groups of the amino acid residues Ser, Thr or Tyr, the ε-amino group of Lys, the SH group of Cys or the carboxyl group of Asp and Glu. The polypeptide and the lipophilic compound may be conjugated to each other either directly or by use of a linker. The lipophilic compound may be a natural compound such as a saturated or unsaturated fatty acid, a fatty acid diketone, a terpene, a prostaglandin, a vitamin, a carotenoid or steroid, or a synthetic compound such as a carbon acid, an alcohol, an amine and sulphonic acid with one or more alkyl, aryl, alkenyl or other multiple unsaturated compounds. The conjugation between the polypeptide and the lipophilic compound, optionally through a linker may be done according to methods known in the art, e.g. as

described by Bodanszky in Peptide Synthesis, John Wiley, New York, 1976 and in WO 96/12505.

Conjugation to a polymer molecule

The polymer molecule to be coupled to the polypeptide may be any suitable polymer molecule, such as a natural or synthetic homo-polymer or heteropolymer, typically with a molecular weight in the range of about 300-100,000 Da, such as about 1000-50,000 Da, e.g. in the range of about 1000- 40,000 Da. More particularly, the polymer molecule, such as PEG, in particular mPEG, will typically have a molecular weight of about 2, 5, 10, 12, 15, 20, 30, 40 or 50 kDa, in particular a molecular weight of about 5 kDa, about 10 kDa, about 12 kDa, about 15 kDa, about 20 kDa, about 30 kDa or about 40 kDa. The PEG molecule may be branched (e.g., mPEG2), or may be unbranched (i.e., linear).

When used about polymer molecules herein, the word “about” indicates an approximate average molecular weight and reflects the fact that there will normally be a certain molecular weight distribution in a given polymer preparation.

Examples of homo-polymers include a polyol (i.e. poly-OH), a polyamine (i.e. poly-NH_2) and a polycarboxylic acid (i.e. poly-COOH). A hetero- polymer is a polymer which comprises one or more different coupling groups, such as a hydroxyl group and an amine group.

Examples of suitable polymer molecules include polymer molecules selected from the group consisting of polyalkylene oxide (PAO), including polyalkylene glycol (PAG), such as polyethylene glycol (PEG) and polypropylene glycol (PPG), branched PEGs (PEG2), poly-vinyl alcohol (PVA), poly-carboxylate, poly-(vinylpyrolidone), polyethylene-co-maleic acid anhydride, polystyrene-co-malic acid anhydride, dextran including carboxymethyl-dextran, or any other biopolymer suitable for reducing immunogenicity and/or increasing functional *in vivo* half-life and/or serum half-life. Generally, polyalkylene glycol-derived polymers are biocompatible, non-toxic, non-antigenic, non-immunogenic, have various water solubility properties, and are easily excreted from living organisms.

PEG is the preferred polymer molecule to be used, since it has only few reactive groups capable of cross-linking compared to e.g. polysaccharides such as dextran. In particular, monofunctional PEG, e.g. monomethoxypolyethylene glycol (mPEG), is of

interest since its coupling chemistry is relatively simple (only one reactive group is available for conjugating with attachment groups on the polypeptide). Consequently, the risk of cross-linking is eliminated, the resulting polypeptide conjugates are more homogeneous and the reaction of the polymer molecules with the polypeptide is easier to control.

To effect covalent attachment of the polymer molecule(s) to the polypeptide, the hydroxyl end groups of the polymer molecule must be provided in activated form, i.e. with reactive functional groups (examples of which include primary amino groups, hydrazide (HZ), thiol, succinate (SUC), succinimidyl succinate (SS), succinimidyl succinamide (SSA), succinimidyl propionate (SPA), succinimidyl butanoate (SBA), succinimidyl carboxymethylate (SCM), benzotriazole carbonate (BTC), N-hydroxysuccinimide (NHS), aldehyde, nitrophenylcarbonate (NPC), and tresylate (TRES)). Suitably activated polymer molecules are commercially available, e.g. from Nektar Therapeutics, Inc., Huntsville, AL, USA; PolyMASC Pharmaceuticals plc, UK; or SunBio Corporation, Anyang City, South Korea. Alternatively, the polymer molecules can be activated by conventional methods known in the art, e.g. as disclosed in WO 90/13540. Specific examples of activated linear or branched polymer molecules suitable for use in the present invention are described in the Nektar Therapeutics, Inc. 2003 Catalog ("Nektar Molecule Engineering: Polyethylene Glycol and Derivatives for Advanced Pegylation, Catalog 2003"), incorporated by reference herein. Specific examples of activated PEG polymers include the following linear PEGs: NHS-PEG , SPA-PEG, SSPA-PEG, SBA-PEG, SS-PEG, SSA-PEG, SC-PEG, SG-PEG, SCM-PEG, NOR-PEG, BTC-PEG, EPOX-PEG, NCO-PEG, NPC-PEG, CDI-PEG, ALD-PEG, TRES-PEG, VS-PEG, OPSS-PEG, IODO-PEG, and MAL-PEG, and branched PEGs, such as PEG2-NHS, PEG2-MAL, and those disclosed in US 5,932,462 and US 5,643,575, both of which are incorporated herein by reference. Furthermore, the following publications, incorporated herein by reference, disclose useful polymer molecules and/or PEGylation chemistries: US 5,824,778, US 5,476,653, WO 97/32607, EP 229,108, EP 402,378, US 4,902,502, US 5,281,698, US 5,122,614, US 5,219,564, WO 92/16555, WO 94/04193, WO 94/14758, WO 94/17039, WO 94/18247, WO 94/28024, WO 95/00162, WO 95/11924, WO95/13090, WO 95/33490, WO 96/00080, WO 97/18832, WO 98/41562, WO 98/48837, WO 99/32134, WO 99/32139, WO 99/32140,

WO 96/40791, WO 98/32466, WO 95/06058, EP 439 508, WO 97/03106, WO 96/21469, WO 95/13312, EP 921 131, US 5,736,625, WO 98/05363, EP 809 996, US 5,629,384, WO 96/41813, WO 96/07670, US 5,473,034, US 5,516,673, EP 605 963, US 5,382,657, EP 510 356, EP 400 472, EP 183 503 and EP 154 316.

The conjugation of the polypeptide and the activated polymer molecules is conducted by use of any conventional method, e.g. as described in the following references (which also describe suitable methods for activation of polymer molecules): Harris and Zalipsky, eds., Poly(ethylene glycol) Chemistry and Biological Applications, AZC, Washington; R.F. Taylor, (1991), "Protein immobilisation. Fundamental and applications", Marcel Dekker, N.Y.; S.S. Wong, (1992), "Chemistry of Protein Conjugation and Crosslinking", CRC Press, Boca Raton; G.T. Hermanson et al., (1993), "Immobilized Affinity Ligand Techniques", Academic Press, N.Y.

For PEGylation of cysteine residues the polypeptide is usually treated with a reducing agent, such as dithiothreitol (DDT) prior to PEGylation. The reducing agent is subsequently removed by any conventional method, such as by desalting. Conjugation of PEG to a cysteine residue typically takes place in a suitable buffer at pH 6-9 at temperatures varying from 4°C to 25°C for periods up to about 16 hours. Examples of activated PEG polymers for coupling to cysteine residues include the following linear and branched PEGs: vinylsulfone-PEG (PEG-VS), such as vinylsulfone-mPEG (mPEG-VS); orthopyridyl-disulfide-PEG (PEG-OPSS), such as orthopyridyl-disulfide-mPEG (mPEG-OPSS); and maleimide-PEG (PEG-MAL), such as maleimide-mPEG (mPEG-MAL) and branched maleimide-mPEG2 (mPEG2-MAL).

Pegylation of lysines often employs PEG-N-hydroxylsuccinimide (e.g., mPEG-NHS or mPEG2-NHS), or esters such as PEG succinimidyl propionate (e.g., mPEG-SPA) or PEG succinimidyl butanoate (e.g., mPEG-SBA). One or more PEGs can be attached to a protein within 30 minutes at pH 8–9.5 at room temperature if about equimolar amounts of PEG and protein are mixed. A molar ratio of PEG to protein amino groups of 1–5 to 1 will usually suffice. Increasing pH increases the rate of reaction, while lowering pH reduces the rate of reaction. These highly reactive active esters can couple at physiological pH, but less reactive derivatives typically require higher pH. Low temperatures may also be employed if a labile protein is being used. Under low temperature conditions, a longer reaction time may be used.

N-terminal PEGylation is facilitated by the difference between the pKa values of the α-amino group of the N-terminal amino acid (~7.6 to 8.0) and the ε-amino group of lysine (~10). PEGylation of the N-terminal amino group often employs PEG-aldehydes (such as mPEG-propionaldehyde or mPEG-butylaldehyde), which are more selective for amines and thus are less likely to react with the imidazole group of histidine; in addition, PEG reagents used for lysine conjugation (such as mPEG-SPA, mPEG-SBA, or mPEG-NHS) may also be used for conjugation of the N-terminal amine. Conjugation of a PEG-aldehyde to the N-terminal amino group typically takes place in a suitable buffer (such as, 100 mM sodium acetate or 100 mM sodium bisphosphate buffer with 20 mM sodium cyanoborohydride) at pH ~ 5.0 overnight at temperatures varying from about 4°C to 25°C. Useful N-terminal PEGylation methods and chemistries are also described in US Pat. 5,985,265 and US Pat. 6,077,939, both incorporated herein by reference.

Typically, linear PEG or mPEG polymers will have a molecular weight of about 5 kDa, about 10 kDa, about 12 kDa, about 15 kDa, about 20 kDa, or about 30 kDa. Branched PEG (PEG2 or mPEG2) polymers will typically have a molecular weight of about 10 kDa, about 20 kDa, or about 40 kDa. In some instances, the higher-molecular weight branched PEG2 reagents, such as 20 kDa or 40 kDa PEG2, including e.g. mPEG2-NHS for lysine PEGylation, mPEG2-MAL for cysteine PEGylation, or MPEG2-aldehyde for N-terminal PEGylation (all available from Nektar Therapeutics, Inc, Huntsville AL), may be used. The branched structure of the PEG2 compound results in a relatively large molecular volume, so fewer attached molecules (or, one attached molecule) may impart the desired characteristics of the PEGylated molecule.

The skilled person will be aware that the activation method and/or conjugation chemistry to be used depends on the attachment group(s) of the interferon-alpha polypeptide as well as the functional groups of the polymer (e.g., being amino, hydroxyl, carboxyl, aldehyde or sulfhydryl). The PEGylation may be directed towards conjugation to all available attachment groups on the polypeptide (i.e. such attachment groups that are exposed at the surface of the polypeptide) or may be directed towards specific attachment groups, e.g. cysteine residues, lysine residues, or the N-terminal amino group. Furthermore, the conjugation may be achieved in one step or in a stepwise manner (e.g. as described in WO 99/55377).

In some instances, the polymer conjugation is performed under conditions aiming at reacting as many of the available polymer attachment groups as possible with polymer molecules. This is achieved by means of a suitable molar excess of the polymer in relation to the polypeptide. Typical molar ratios of activated polymer molecules to polypeptide are up to about 1000-1, such as up to about 200-1 or up to about 100-1. In some cases, the ratio may be somewhat lower, however, such as up to about 50-1, 10-1 or 5-1. Also equimolar ratios may be used.

It is also contemplated according to the invention to couple the polymer molecules to the polypeptide through a linker. Suitable linkers are well known to the skilled person. A preferred example is cyanuric chloride (Abuchowski et al., (1977), J. Biol. Chem., 252, 3578-3581; US 4,179,337; Shafer et al., (1986), J. Polym. Sci. Polym. Chem. Ed., 24, 375-378).

Subsequent to the conjugation residual activated polymer molecules are blocked according to methods known in the art, e.g. by addition of primary amine to the reaction mixture, and the resulting inactivated polymer molecules removed by a suitable method.

Covalent *in vitro* coupling of a sugar moiety to amino acid residues of interferon-alpha may be used to modify or increase the number or profile of sugar substituents. Depending on the coupling mode used, the carbohydrate(s) may be attached to a) arginine and histidine (Lundblad and Noyes, Chemical Reagents for Protein Modification, CRC Press Inc. Boca Raton, Fl), b) free carboxyl groups (e.g. of the C-terminal amino acid residue, asparagine or glutamine), c) free sulfhydryl groups such as that of cysteine, d) free hydroxyl groups such as those of serine, threonine, tyrosine or hydroxyproline, e) aromatic residues such as those of phenylalanine or tryptophan or f) the amide group of glutamine. These amino acid residues constitute examples of attachment groups for a sugar moiety, which may be introduced and/or removed in the interferon-alpha polypeptide. Suitable methods of *in vitro* coupling are described in WO 87/05330 and in Aplin et al., CRC Crit Rev. Biochem., pp. 259-306, 1981. The *in vitro* coupling of sugar moieties or PEG to protein- and peptide-bound Gln-residues can also be carried out by transglutaminases (TGases), e.g. as described by Sato et al., 1996 *Biochemistry* 35, 13072-13080 or in EP 725145.

Coupling to a sugar moiety

In order to achieve *in vivo* glycosylation of an interferon-alpha polypeptide that has been modified by introduction of one or more glycosylation sites, the nucleotide sequence encoding the polypeptide part of the conjugate is inserted in a glycosylating, eukaryotic expression host. The expression host cell may be selected from fungal (filamentous fungal or yeast), insect, mammalian animal cells, from transgenic plant cells or from transgenic animals. Furthermore, the glycosylation may be achieved in the human body when using a nucleotide sequence encoding the polypeptide part of a conjugate of the invention or a polypeptide of the invention in gene therapy. In one aspect the host cell is a mammalian cell, such as a CHO cell, a COS cell, a BHK or HEK cell, e.g. HEK293, or an insect cell, such as an SF9 cell, or a yeast cell, e.g. *Saccharomyces cerevisiae, Pichia pastoris* or any other suitable glycosylating host, e.g. as described further below. Optionally, sugar moieties attached to the interferon-α polypeptide by *in vivo* glycosylation are further modified by use of glycosyltransferases, e.g. using the GlycoAdvance™ technology marketed by Neose, Horsham, PA, USA. Thereby, it is possible to, e.g., increase the sialyation of the glycosylated interferon-alpha polypeptide following expression and *in vivo* glycosylation by CHO cells.

Coupling to an organic derivatizing agent

Covalent modification of the interferon-alpha polypeptide may be performed by reacting (an) attachment group(s) of the polypeptide with an organic derivatizing agent. Suitable derivatizing agents and methods are well known in the art. For example, cysteinyl residues most commonly are reacted with α-haloacetates (and corresponding amines), such as chloroacetic acid or chloroacetamide, to give carboxymethyl or carboxyamidomethyl derivatives. Cysteinyl residues also are derivatized by reaction with bromotrifluoroacetone, α-bromo-β-(4-imidozoyl)propionic acid, chloroacetyl phosphate, N-alkylmaleimides, 3-nitro-2-pyridyl disulfide, methyl 2-pyridyl disulfide, p-chloromercuribenzoate, 2-chloromercuri-4-nitrophenol, or chloro-7-nitrobenzo-2-oxa-1,3-diazole. Histidyl residues are derivatized by reaction with diethylpyrocarbonate at pH 5.5-7.0 because this agent is relatively specific for the histidyl side chain. Para-bromophenacyl bromide is also useful; the reaction is preferably performed in 0.1 M sodium cacodylate at pH 6.0. Lysinyl and amino terminal residues are reacted with

succinic or other carboxylic acid anhydrides. Derivatization with these agents has the effect of reversing the charge of the lysinyl residues. Other suitable reagents for derivatizing α-amino-containing residues include imidoesters such as methyl picolinimidate; pyridoxal phosphate; pyridoxal; chloroborohydride; trinitrobenzenesulfonic acid; O-methylisourea; 2,4-pentanedione; and transaminase-catalyzed reaction with glyoxylate. Arginyl residues are modified by reaction with one or several conventional reagents, among them phenylglyoxal, 2,3-butanedione, 1,2-cyclohexanedione, and ninhydrin. Derivatization of arginine residues requires that the reaction be performed in alkaline conditions because of the high pKa of the guanidine functional group. Furthermore, these reagents may react with the groups of lysine as well as the arginine guanidino group. Carboxyl side groups (aspartyl or glutamyl or C-terminal amino acid residue) are selectively modified by reaction with carbodiimides (R-N=C=N-R'), where R and R' are different alkyl groups, such as 1-cyclohexyl-3-(2-morpholinyl-4-ethyl) carbodiimide or 1-ethyl-3-(4-azonia-4,4-dimethylpentyl) carbodiimide. Furthermore, aspartyl and glutamyl residues are converted to asparaginyl and glutaminyl residues by reaction with ammonium ions.

Blocking of a functional site

Since excessive polymer conjugation may lead to a loss of activity of the interferon-α polypeptide to which the polymer is conjugated, it may be advantageous to remove attachment groups located at the functional site or to block the functional site prior to conjugation. These latter strategies constitute further aspects of the invention (the first strategy being exemplified further above, e.g. by removal of lysine residues which may be located close to a functional site). More specifically, according to the second strategy the conjugation between the interferon-alpha polypeptide and the non-polypeptide moiety is conducted under conditions where the functional site of the polypeptide is blocked by a helper molecule capable of binding to the functional site of the polypeptide. Preferably, the helper molecule is one which specifically recognizes a functional site of the polypeptide, such as a receptor, in particular the type I interferon receptor. Alternatively, the helper molecule may be an antibody, in particular a monoclonal antibody recognizing the interferon-alpha polypeptide. In particular, the helper molecule may be a neutralizing monoclonal antibody.

The polypeptide is allowed to interact with the helper molecule before effecting conjugation. This ensures that the functional site of the polypeptide is shielded or protected and consequently unavailable for derivatization by the non-polypeptide moiety such as a polymer. Following its elution from the helper molecule, the conjugate between the non-polypeptide moiety and the polypeptide can be recovered with at least a partially preserved functional site.

The subsequent conjugation of the polypeptide having a blocked functional site to a polymer, a lipophilic compound, an organic derivatizing agent or any other compound is conducted in the normal way, e.g. as described in the sections above entitled "*Conjugation to ....*".

Irrespective of the nature of the helper molecule to be used to shield the functional site of the polypeptide from conjugation, it is desirable that the helper molecule is free from or comprises only a few attachment groups for the non-polypeptide moiety of choice in parts of the molecule where the conjugation to such groups would hamper the desorption of the conjugated polypeptide from the helper molecule. Hereby, selective conjugation to attachment groups present in non-shielded parts of the polypeptide can be obtained and it is possible to reuse the helper molecule for repeated cycles of conjugation. For instance, if the non-polypeptide moiety is a polymer molecule such as PEG, which has the epsilon amino group of a lysine or N-terminal amino acid residue as an attachment group, it is desirable that the helper molecule is substantially free from conjugatable epsilon amino groups, preferably free from any epsilon amino groups. Accordingly, in some instances the helper molecule is a protein or peptide capable of binding to the functional site of the polypeptide, which protein or peptide is free from any conjugatable attachment groups for the non-polypeptide moiety of choice.

In a further aspect the helper molecule is first covalently linked to a solid phase such as column packing materials, for instance Sephadex or agarose beads, or a surface, e.g. reaction vessel. Subsequently, the polypeptide is loaded onto the column material carrying the helper molecule and conjugation carried out according to methods known in the art, e.g. as described in the sections above entitled "Conjugation to ....". This procedure allows the polypeptide conjugate to be separated from the helper molecule by elution. The polypeptide conjugate is eluted by conventional techniques under physico-chemical conditions that do not lead to a substantive degradation of the polypeptide

conjugate. The fluid phase containing the polypeptide conjugate is separated from the solid phase to which the helper molecule remains covalently linked. The separation can be achieved in other ways: For instance, the helper molecule may be derivatized with a second molecule (e.g. biotin) that can be recognized by a specific binder (e.g. streptavidin). The specific binder may be linked to a solid phase thereby allowing the separation of the polypeptide conjugate from the helper molecule-second molecule complex through passage over a second helper-solid phase column which will retain, upon subsequent elution, the helper molecule-second molecule complex, but not the polypeptide conjugate. The polypeptide conjugate may be released from the helper molecule in any appropriate fashion. De-protection may be achieved by providing conditions in which the helper molecule dissociates from the functional site of the interferon-α to which it is bound. For instance, a complex between an antibody to which a polymer is conjugated and an anti-idiotypic antibody can be dissociated by adjusting the pH to an acid or alkaline pH.

Conjugation of a tagged interferon-alpha polypeptide

In another aspect the interferon-alpha polypeptide is expressed as a fusion protein with a tag, i.e. an amino acid sequence or peptide made up of typically 1-30, such as 1-20 or 1-15 or 1-10 or 1-5 amino acid residues, e.g. added to the N-terminus or to the C-terminus of the polypeptide. Besides allowing for fast and easy purification, the tag is a convenient tool for achieving conjugation between the tagged polypeptide and the non-polypeptide moiety. In particular, the tag may be used for achieving conjugation in microtiter plates or other carriers, such as paramagnetic beads, to which the tagged polypeptide can be immobilised via the tag. The conjugation to the tagged polypeptide in, e.g., microtiter plates has the advantage that the tagged polypeptide can be immobilised in the microtiter plates directly from the culture broth (in principle without any purification) and subjected to conjugation. Thereby, the total number of process steps (from expression to conjugation) can be reduced. Furthermore, the tag may function as a spacer molecule ensuring an improved accessibility to the immobilised polypeptide to be conjugated. The conjugation using a tagged polypeptide may be to any of the non-polypeptide moieties disclosed herein, e.g. to a polymer molecule such as PEG.

The identity of the specific tag to be used is not critical as long as the tag is capable of being expressed with the polypeptide and is capable of being immobilised on a suitable surface or carrier material. A number of suitable tags are commercially available, e.g. from Unizyme Laboratories, Denmark. Antibodies against such tags are commercially available, e.g. from ADI, Aves Lab and Research Diagnostics.

POLYNUCLEOTIDES OF THE INVENTION

The invention provides isolated or recombinant nucleic acids (also referred to herein as polynucleotides), collectively referred to as "nucleic acids (or polynucleotides) of the invention", which encode polypeptides of the invention. The polynucleotides of the invention are useful in a variety of applications. As discussed above, the polynucleotides are useful in producing polypeptides of the invention. In addition, polynucleotides of the invention can be incorporated into expression vectors useful for gene therapy, DNA vaccination, and immunotherapy, as described in more detail below.

In one aspect, the invention provides isolated or recombinant polynucleotides that each comprise a nucleic acid sequence which encodes a polypeptide comprising an amino acid sequence selected from SEQ ID NO:1- SEQ ID NO:319; or, a complementary nucleic acid sequence thereof.

The invention also provides isolated or recombinant polynucleotides that each comprise a nucleic acid sequence which encodes a polypeptide comprising an amino acid sequence which (a) differs in 0 to 16 amino acid positions (such as in 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, or 16 amino acid positions, e.g., in 0-15 amino acid positions, in 0-14 amino acid positions, in 0-13 amino acid positions, in 0-12 amino acid positions, 0-11 amino acid positions, in 0-10 amino acid positions, in 0-9 amino acid positions, in 0-8 amino acid positions, in 0-7 amino acid positions, in 0-6 amino acid positions, in 0-5 amino acid positions, in 0-4 amino acid positions, in 0-3 amino acid positions, in 0-2 amino acid positions or in 0-1 amino acid positions) from one of SEQ ID NO:1-SEQ ID NO:319, or, a complementary nucleic acid sequence thereof. Some polypeptides encoded by polynucleotides of the invention further comprise one or more additional amino acid(s), such as a methionine added to the N-terminus. In some instances the encoded polypeptide exhibits an interferon-alpha activity.

The invention also provides isolated or recombinant polynucleotides that each comprise a nucleic acid sequence which encodes a polypeptide comprising an amino acid sequence having at least 90% sequence identity (e.g., at least about 91%, at least about 92%, at least about 93%, at least about 94%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, or at least about 99% amino acid sequence identity) to any one of SEQ ID NOs:1-319, or, a complementary nucleic acid sequence thereof. Some polypeptides encoded by polynucleotides of the invention further comprise one or more additional amino acid(s), such as a methionine added to the N-terminus. In some instances the encoded polypeptide exhibits an interferon-alpha activity.

Additional Aspects

Any of the polynucleotides of the invention (which includes those described above) may encode a fusion protein comprising at least one additional amino acid sequence, such as, for example, a secretion/localization sequence, a sequence useful for solubilization or immobilization (e.g., for cell surface display) of the polypeptide, a sequence useful for detection and/or purification of the polypeptide (e.g., a polypeptide purification subsequence, such as an epitope tag, a polyhistidine sequence, and the like), or a sequence useful for stabilizing or extending the in vivo half life of the protein (such as an Ig fusion or an albumin fusion).

In another aspect, the invention provides cells comprising one or more of the polynucleotides of the invention. Such cells may express one or more polypeptides encoded by the polynucleotides of the invention.

The invention also provides vectors comprising any of the polynucleotides of the invention. Such vectors may comprise a plasmid, a cosmid, a phage, a virus, or a fragment of a virus. Such vectors may comprise an expression vector, and, if desired, the nucleic acid is operably linked to a promoter, including those discussed herein and below. Furthermore, in another aspect, the invention provides compositions comprising an excipient or carrier and at least one of any of the polynucleotides of the invention, or vectors, cells, or host comprising such nucleic acids. Such composition may be pharmaceutical compositions, and the excipient or carrier may be a pharmaceutically acceptable excipient or carrier.

The invention also includes compositions comprising two or more nucleic acids of the invention, or fragments thereof (e.g., as substrates for recombination). The composition can comprise a library of recombinant nucleic acids, where the library contains at least 2, at least 3, at least 5, at least 10, at least 20, at least 50, or at least 100 or more nucleic acids described above. The nucleic acids are optionally cloned into expression vectors, providing expression libraries.

The polynucleotides of the invention and fragments thereof, as well as vectors comprising such polynucleotides, may be employed for therapeutic or prophylactic uses in combination with a suitable carrier, such as a pharmaceutical carrier. Such compositions comprise a therapeutically and/or prophylactically effective amount of the compound, and a pharmaceutically acceptable carrier or excipient. Such a carrier or excipient includes, but is not limited to, saline, buffered saline, dextrose, water, glycerol, ethanol, and combinations thereof. The formulation should suit the mode of administration. Methods of administering nucleic acids, polypeptides, and proteins are well known in the art, and are further discussed below.

The invention also includes compositions produced by digesting one or more of any of the nucleic acids of the invention with a restriction endonuclease, an RNAse, or a DNAse (e.g., as is performed in certain of the recombination formats noted above); and compositions produced by fragmenting or shearing one or more nucleic acids of the invention by mechanical means (e.g., sonication, vortexing, and the like), which can also be used to provide substrates for recombination in the methods described herein. The invention also provides compositions produced by cleaving at least one of any of the nucleic acids of the invention. The cleaving may comprise mechanical, chemical, or enzymatic cleavage, and the enzymatic cleavage may comprise cleavage with a restriction endonuclease, an RNAse, or a DNAse.

Also included in the invention are compositions produced by a process comprising incubating one or more of the fragmented nucleic acids of the invention in the presence of ribonucleotide or deoxyribonucleotide triphosphates and a nucleic acid polymerase. This resulting composition forms a recombination mixture for many of the recombination formats noted above. The nucleic acid polymerase may be an RNA polymerase, a DNA polymerase, or an RNA-directed DNA polymerase (e.g., a "reverse transcriptase"); the polymerase can be, e.g., a thermostable DNA polymerase (e.g., VENT, TAQ, or the like).

Similarly, compositions comprising sets of oligonucleotides corresponding to more than one nucleic acids of the invention are useful as recombination substrates and are a feature of the invention. For convenience, these fragmented, sheared, or oligonucleotide synthesized mixtures are referred to as fragmented nucleic acid sets.

The invention also provides an isolated or recombinant nucleic acid encoding a polypeptide that exhibits an interferon-alpha activity, produced by mutating or recombining at least one nucleic acid of the invention.

Making Polynucleotides

Polynucleotides, oligonucleotides, and nucleic acid fragments of the invention can be prepared by standard solid-phase methods, according to known synthetic methods. Typically, fragments of up to about 100 bases are individually synthesized, then joined (e.g., by enzymatic or chemical ligation methods, or polymerase mediated recombination methods) to form essentially any desired continuous sequence. For example, the polynucleotides and oligonucleotides of the invention can be prepared by chemical synthesis using, e.g., classical phosphoramidite method described by, e.g., Beaucage et al. (1981) Tetrahedron Letters 22:1859-1869, or the method described by Matthes et al. (1984) EMBO J 3:801-805, e.g., as is typically practiced in automated synthetic methods. According to the phosphoramidite method, oligonucleotides are synthesized, e.g., in an automatic DNA synthesizer, purified, annealed, ligated and cloned into appropriate vectors.

In addition, essentially any polynucleotide can be custom ordered from any of a variety of commercial sources, such as Operon Biotechnologies Inc. (Huntsville, AL) and many others. Similarly, peptides and antibodies can be custom ordered from any of a variety of commercial sources, such as AnaSpec, Inc. (San Jose, CA).

Certain polynucleotides of the invention may also be obtained by screening cDNA libraries (e.g., libraries generated by recombining homologous nucleic acids as in typical recursive sequence recombination methods) using oligonucleotide probes that can hybridize to or PCR-amplify polynucleotides which encode interferon-alpha polypeptides and fragments of those polypeptides. Procedures for screening and isolating cDNA clones are well-known to those of skill in the art. Such techniques are described in, e.g., Berger and Kimmel, Guide to Molecular Cloning Techniques, Methods in Enzymol. Vol.

152, Acad. Press, Inc., San Diego, CA ("Berger"); Sambrook, *supra*, and Current Protocols in Molecular Biology, Ausubel, *supra*. Some polynucleotides of the invention can be obtained by altering a naturally occurring sequence, e.g., by mutagenesis, recursive sequence recombination (e.g., shuffling), or oligonucleotide recombination. In other cases, such polynucleotides can be made in silico or through oligonucleotide recombination methods as described in the references cited herein.

As described in more detail herein, the polynucleotides of the invention include polynucleotides that encode polypeptides of the invention, polynucleotide sequences complementary to these polynucleotide sequences, and polynucleotides that hybridize under at least stringent conditions to the sequences defined herein. A coding sequence refers to a polynucleotide sequence encoding a particular polypeptide or domain, region, or fragment of said polypeptide. A coding sequence may encode (code for) a polypeptide of the invention exhibiting an interferon alpha activity as described above. The polynucleotides of the invention may be in the form of RNA or in the form of DNA, and include mRNA, cRNA, synthetic RNA and DNA, and cDNA. The polynucleotides may be double-stranded or single-stranded, and if single-stranded, can be the coding strand or the non-coding (anti-sense, complementary) strand. The polynucleotides of the invention include the coding sequence of a polypeptide of the invention (i) in isolation, (ii) in combination with one or more additional coding sequences, so as to encode, e.g., a fusion protein, a pre-protein, a prepro-protein, or the like, (iii) in combination with non-coding sequences, such as introns, control elements, such as a promoter (e.g., naturally occurring or recombinant or shuffled promoter), a terminator element, or 5' and/or 3' untranslated regions effective for expression of the coding sequence in a suitable host, and/or (iv) in a vector, cell, or host environment in which the coding sequence is a heterologous gene.

Polynucleotides of the invention can also be found in combination with typical compositional formulations of nucleic acids, including in the presence of carriers, buffers, adjuvants, excipients, and the like, as are known to those of ordinary skill in the art. Polynucleotide fragments typically comprise at least about 200 nucleotide bases, such as at least about 250, 300, 350, 400, 450, 460, 470, or more bases. The nucleotide fragments of polynucleotides of the invention may hybridize under highly stringent conditions to a polynucleotide sequence described herein and/or encode amino acid sequences having at least one of the properties of polypeptides of the invention described herein.

Modified Coding Sequences

As will be understood by those of ordinary skill in the art, it can be advantageous to modify a coding sequence to enhance its expression in a particular host. The genetic code is redundant with 64 possible codons, but most organisms preferentially use a subset of these codons. The codons that are utilized most often in a species are considered optimal codons, and those not utilized very often are classified as rare or low-usage codons (see, e.g., Zhang, S. P. et al. (1991) Gene 105:61-72). Codons can be substituted to reflect the preferred codon usage of the host, a process sometimes termed "codon optimization" or "controlling for species codon bias."

Modified coding sequence containing codons preferred by a particular prokaryotic or eukaryotic host (see, e.g., Murray, E. et al. (1989) Nuc Acids Res 17:477-508; Griswold et al., (2003) Protein Expr. Purif. 27(1):134-42) can be prepared, for example, to increase the rate of translation or to produce recombinant RNA transcripts having desirable properties, such as a longer half-life, as compared with transcripts produced from a non-optimized sequence. Translation stop codons can also be modified to reflect host preference. For example, preferred stop codons for *S. cerevisiae* and mammals are UAA and UGA respectively. The preferred stop codon for monocotyledonous plants is UGA, whereas insects and *E. coli* prefer to use UAA as the stop codon (Dalphin, M.E. et al. (1996) Nucl. Acids Res. 24:216-218).

The polynucleotide sequences of the present invention can be engineered in order to alter a coding sequence of the invention for a variety of reasons, including but not limited to, alterations which modify the cloning, processing and/or expression of the gene product. For example, alterations may be introduced using techniques which are well known in the art, e.g., site-directed mutagenesis, to insert new restriction sites, to alter glycosylation patterns, to introduce or remove attachment groups (e.g., for pegylation or other conjugation), to change codon preference, to introduce splice sites, etc.

Silent Variations

Because of the degeneracy of the genetic code, a large number of functionally identical nucleic acids encode any given polypeptide. For instance, inspection of the codon table below (Table 3) shows that codons AGA, AGG, CGA, CGC, CGG, and CGU all encode the amino acid arginine. Thus, at every position in a nucleic acid sequence

where an arginine is specified by a codon, the codon can be altered to any of the corresponding codons described above without altering the encoded polypeptide. Such nucleic acid variations are "silent variations". It is to be understood that U in an RNA sequence corresponds to T in a DNA sequence.

Table 3
Codon Table

Amino acid			Codon(s)					
Alanine	Ala	A	GCA	GCC	GCG	GCU		
Cysteine	Cys	C	UGC	UGU				
Aspartic acid	Asp	D	GAC	GAU				
Glutamic acid	Glu	E	GAA	GAG				
Phenylalanine	Phe	F	UUC	UUU				
Glycine	Gly	G	GGA	GGC	GGG	GGU		
Histidine	His	H	CAC	CAU				
Isoleucine	Ile	I	AUA	AUC	AUU			
Lysine	Lys	K	AAA	AAG				
Leucine	Leu	L	UUA	UUG	CUA	CUC	CUG	CUU
Methionine	Met	M	AUG					
Asparagine	Asn	N	AAC	AAU				
Proline	Pro	P	CCA	CCC	CCG	CCU		
Glutamine	Gln	Q	CAA	CAG				
Arginine	Arg	R	AGA	AGG	CGA	CGC	CGG	CGU
Serine	Ser	S	AGC	AGU	UCA	UCC	UCG	UCU
Threonine	Thr	T	ACA	ACC	ACG	ACU		
Valine	Val	V	GUA	GUC	GUG	GUU		
Tryptophan	Trp	W	UGG					
Tyrosine	Tyr	Y	UAC	UAU				

It will thus be appreciated by those skilled in the art that due to the degeneracy of the genetic code, a multitude of nucleic acids sequences encoding polypeptides of the invention may be produced, some of which may bear minimal sequence identity to the

nucleic acid sequences explicitly disclosed herein. One of ordinary skill in the art will recognize that each codon in a nucleic acid (except AUG and UGC, which are ordinarily the only codon for methionine and tryptophan, respectively) can be modified by standard techniques to encode a functionally identical polypeptide. Accordingly, each silent variation of a nucleic acid which encodes a polypeptide is implicit in any described sequence. The invention also provides each and every possible variation of a nucleic acid sequence encoding a polypeptide of the invention that can be made by selecting combinations based on possible codon choices. These combinations are made in accordance with the standard triplet (codon) genetic code (e.g., as set forth in Table 5), as applied to the nucleic acid sequence encoding a polypeptide of the invention. All such variations of every nucleic acid herein are specifically provided and described by consideration of the sequence in combination with the genetic code. One of skill is fully able to generate any silent substitution of the sequences listed herein.

Using Polynucleotides

The polynucleotides of the invention have a variety of uses in, for example, recombinant production (i.e., expression) of the polypeptides of the invention typically through expression of a plasmid expression vector comprising a sequence encoding the polypeptide or fragment thereof; as therapeutics; as prophylactics; as diagnostic tools; as immunogens; as adjuvants; as diagnostic probes for the presence of complementary or partially complementary nucleic acids (including for detection of a wild-type interferon-alpha nucleic acid), as substrates for further reactions, e.g., recursive sequence recombination reactions or mutation reactions to produce new and/or improved variants, and the like.

Vectors, Promoters, and Expression Systems

The present invention also includes recombinant constructs comprising one or more of the nucleic acid sequences as broadly described above. The constructs comprise a vector, such as, a plasmid, a cosmid, a phage, a virus, a bacterial artificial chromosome (BAC), a yeast artificial chromosome (YAC), and the like, into which a nucleic acid sequence of the invention has been inserted, in a forward or reverse orientation. In some instances, the construct further comprises regulatory sequences, including, for example, a

promoter, operably linked to the nucleic acid sequence. Large numbers of suitable vectors and promoters are known to those of skill in the art, and are commercially available.

General texts that describe molecular biological techniques useful herein, including the use of vectors, promoters and many other relevant topics, include Berger, *supra*; Sambrook (1989), *supra*, and Ausubel, *supra*. Examples of techniques sufficient to direct persons of skill through *in vitro* amplification methods, including the polymerase chain reaction (PCR) the ligase chain reaction (LCR), Qβ-replicase amplification and other RNA polymerase mediated techniques (e.g., NASBA), e.g., for the production of the homologous nucleic acids of the invention are found in Berger, Sambrook, and Ausubel, all *supra*, as well as Mullis et al. (1987) U.S. Patent No. 4,683,202; PCR Protocols: A Guide to Methods and Applications (Innis et al., eds.) Academic Press Inc. San Diego, CA (1990) ("Innis"); Arnheim & Levinson (October 1, 1990) C&EN 36-47; The Journal Of NIH Research (1991) 3:81-94; (Kwoh et al. (1989) Proc Natl Acad Sci USA 86:1173-1177; Guatelli et al. (1990) Proc Natl Acad Sci USA 87:1874-1878; Lomeli et al. (1989) J Clin Chem 35:1826-1831; Landegren et al. (1988) Science 241:1077-1080; Van Brunt (1990) Biotechnology 8:291-294; Wu and Wallace (1989) Gene 4:560-569; Barringer et al. (1990) Gene 89:117-122, and Sooknanan and Malek (1995) Biotechnology 13:563-564. Improved methods of cloning *in vitro* amplified nucleic acids are described in Wallace et al., U.S. Pat. No. 5,426,039. Improved methods of amplifying large nucleic acids by PCR are summarized in Cheng et al. (1994) Nature 369:684-685 and the references therein, in which PCR amplicons of up to 40 kilobases (kb) are generated. One of skill will appreciate that essentially any RNA can be converted into a double stranded DNA suitable for restriction digestion, PCR expansion and sequencing using reverse transcriptase and a polymerase. See Ausubel, Sambrook and Berger, all *supra*.

The present invention also provides host cells that are transduced with vectors of the invention, and the production of polypeptides of the invention by recombinant techniques. Host cells are genetically engineered (e.g., transduced, transformed or transfected) with the vectors of this invention, which may be, for example, a cloning vector or an expression vector. The vector may be, for example, in the form of a plasmid, a viral particle, a phage, etc. The engineered host cells can be cultured in conventional nutrient media modified as appropriate for activating promoters, selecting transformants, or

amplifying genes. The culture conditions, such as temperature, pH, and the like, are those previously used with the host cell selected for expression, and will be apparent to those skilled in the art and in the references cited herein, including, e.g., Freshney (1994) Culture of Animal Cells, a Manual of Basic Technique, third edition, Wiley- Liss, New York and the references cited therein.

The polypeptides of the invention can also be produced in non-animal cells such as plants, yeast, fungi, bacteria and the like. In addition to Sambrook, Berger and Ausubel, details regarding cell culture are found in, e.g., Payne et al. (1992) Plant Cell and Tissue Culture in Liquid Systems John Wiley & Sons, Inc. New York, NY; Gamborg and Phillips (eds.) (1995) Plant Cell, Tissue and Organ Culture; Fundamental Methods Springer Lab Manual, Springer-Verlag (Berlin Heidelberg NY); Atlas & Parks (eds.) The Handbook of Microbiological Media (1993) CRC Press, Boca Raton, FL.

The polynucleotides of the present invention and fragments thereof may be included in any one of a variety of expression vectors for expressing a polypeptide. Such vectors include chromosomal, nonchromosomal and synthetic DNA sequences, e.g., derivatives of SV40, bacterial plasmids, phage DNA, baculovirus, yeast plasmids, vectors derived from combinations of plasmids and phage DNA, viral DNA such as vaccinia, adenovirus, fowl pox virus, pseudorabies, adeno-associated virus, retroviruses and many others. Any vector that transduces genetic material into a cell, and, if replication is desired, which is replicable and viable in the relevant host can be used.

The nucleic acid sequence in the expression vector is operatively linked to an appropriate transcription control sequence (promoter) to direct mRNA synthesis. Examples of such promoters include: LTR or SV40 promoter, *E. coli* lac or trp promoter, phage lambda P_L promoter, CMV promoter, and other promoters known to control expression of genes in prokaryotic or eukaryotic cells or their viruses. The expression vector also contains a ribosome binding site for translation initiation, and a transcription terminator. The vector optionally includes appropriate sequences for amplifying expression, e.g., an enhancer. In addition, the expression vectors optionally comprise one or more selectable marker genes to provide a phenotypic trait for selection of transformed host cells, such as dihydrofolate reductase or neomycin resistance for eukaryotic cell culture, or such as tetracycline or ampicillin resistance in *E. coli.*

The vector containing the appropriate DNA sequence encoding a polypeptide of the invention, as well as an appropriate promoter or control sequence, may be employed to transform an appropriate host to permit the host to express the polypeptide. Examples of appropriate expression hosts include: bacterial cells, such as *E. coli*, *Streptomyces*, and *Salmonella typhimurium*; fungal cells, such as *Saccharomyces cerevisiae, Pichia pastoris,* and *Neurospora crassa*; insect cells such as *Drosophila* and *Spodoptera frugiperda*; mammalian cells such as CHO, COS, BHK, HEK 293 or Bowes melanoma; plant cells, etc. It is understood that not all cells or cell lines need to be capable of producing fully functional polypeptides of the invention or fragments thereof; for example, antigenic fragments of the polypeptide may be produced in a bacterial or other expression system. The invention is not limited by the host cells employed.

In bacterial systems, a number of expression vectors may be selected depending upon the use intended for the polypeptide or fragment thereof. For example, when large quantities of a polypeptide or fragments thereof are needed for the induction of antibodies, vectors which direct high level expression of fusion proteins that are readily purified may be desirable. Such vectors include, but are not limited to, multifunctional *E. coli* cloning and expression vectors such as BLUESCRIPT (Stratagene), in which the nucleotide coding sequence may be ligated into the vector in-frame with sequences for the amino-terminal Met and the subsequent 7 residues of beta-galactosidase so that a hybrid protein is produced; pIN vectors (Van Heeke & Schuster (1989) J Biol Chem 264:5503-5509); pET vectors (Novagen, Madison WI); and the like.

Similarly, in the yeast *Saccharomyces cerevisiae* a number of vectors containing constitutive or inducible promoters such as alpha factor, alcohol oxidase and PGH may be used for production of the polypeptides of the invention. For reviews, see Ausubel, *supra*, Berger, *supra*, and Grant et al. (1987) Methods in Enzymology 153:516-544.

In mammalian host cells, a number of expression systems, such as viral-based systems, may be utilized. In cases where an adenovirus is used as an expression vector, a coding sequence is optionally ligated into an adenovirus transcription/translation complex consisting of the late promoter and tripartite leader sequence. Insertion in a nonessential E1 or E3 region of the viral genome results in a viable virus capable of expressing a polypeptide of the invention in infected host cells (Logan and Shenk (1984) Proc Natl Acad Sci USA 81:3655-3659). In addition, transcription enhancers, such as the rous

sarcoma virus (RSV) enhancer, are used to increase expression in mammalian host cells. Host cells, media, expression systems, and methods of production include those known for cloning and expression of various mammalian interferon-alphas (e.g., human interferon-alphas).

Additional Expression Elements

Specific initiation signals can aid in efficient translation of a polynucleotide coding sequence of the invention and/or fragments thereof. These signals can include, e.g., the ATG initiation codon and adjacent sequences. In cases where an coding sequence, its initiation codon and upstream sequences are inserted into the appropriate expression vector, no additional translational control signals may be needed. However, in cases where only coding sequence (e.g., a mature protein coding sequence), or a portion thereof, is inserted, exogenous nucleic acid transcriptional control signals including the ATG initiation codon must be provided. Furthermore, the initiation codon must be in the correct reading frame to ensure transcription of the entire insert. Exogenous transcriptional elements and initiation codons can be of various origins, both natural and synthetic. The efficiency of expression can enhanced by the inclusion of enhancers appropriate to the cell system in use (see, e.g., Scharf D. et al. (1994) Results Probl Cell Differ 20:125-62; and Bittner et al. (1987) Methods in Enzymol 153:516-544).

Secretion/Localization Sequences

Polynucleotides encoding polypeptides of the invention can also be fused, for example, in-frame to nucleic acid encoding a secretion/localization sequence, to target polypeptide expression to a desired cellular compartment, membrane, or organelle, or to direct polypeptide secretion to the periplasmic space or into the cell culture media. Such sequences are known to those of skill, and include secretion leader or signal peptides, organelle targeting sequences (e.g., nuclear localization sequences, ER retention signals, mitochondrial transit sequences, chloroplast transit sequences), membrane localization/anchor sequences (e.g., stop transfer sequences, GPI anchor sequences), and the like.

Expression Hosts

In a further aspect, the present invention relates to host cells containing any of the above-described nucleic acids, vectors, or other constructs of the invention. The host cell can be a eukaryotic cell, such as a mammalian cell, a yeast cell, or a plant cell, or the host cell can be a prokaryotic cell, such as a bacterial cell. Introduction of the construct into the host cell can be effected by calcium phosphate transfection, DEAE-Dextran mediated transfection, electroporation, gene or vaccine gun, injection, or other common techniques (see, e.g., Davis, L., Dibner, M., and Battey, I. (1986) Basic Methods in Molecular Biology) for *in vivo, ex vivo* or *in vitro* methods.

A host cell strain is optionally chosen for its ability to modulate the expression of the inserted sequences or to process the expressed protein in the desired fashion. Such modifications of the protein include, but are not limited to, acetylation, carboxylation, glycosylation, phosphorylation, lipidation and acylation. Post-translational processing which cleaves a “pre” or a "prepro" form of the protein may also be important for correct insertion, folding and/or function. Different host cells such as *E. coli*, *Bacillus* sp., yeast or mammalian cells such as CHO, HeLa, BHK, MDCK, HEK 293, WI38, etc. have specific cellular machinery and characteristic mechanisms for such post-translational activities and may be chosen to ensure the correct modification and processing of the introduced foreign protein.

Stable expression can be used for long-term, high-yield production of recombinant proteins. For example, cell lines which stably express a polypeptide of the invention are transduced using expression vectors which contain viral origins of replication or endogenous expression elements and a selectable marker gene. Following the introduction of the vector, cells may be allowed to grow for 1-2 days in an enriched media before they are switched to selective media. The purpose of the selectable marker is to confer resistance to selection, and its presence allows growth and recovery of cells which successfully express the introduced sequences. For example, resistant clumps of stably transformed cells can be proliferated using tissue culture techniques appropriate to the cell type.

Host cells transformed with a nucleotide sequence encoding a polypeptide of the invention are optionally cultured under conditions suitable for the expression and recovery of the encoded protein from cell culture. The polypeptide produced by a

recombinant cell may be secreted, membrane-bound, or contained intracellularly, depending on the sequence and/or the vector used. As will be understood by those of skill in the art, expression vectors containing polynucleotides encoding polypeptides of the invention can be designed with signal sequences which direct secretion of the mature polypeptides through a prokaryotic or eukaryotic cell membrane.

Additional Sequences

The polynucleotides of the present invention optionally comprise a coding sequence fused in-frame to a marker sequence which, e.g., facilitates purification and/or detection of the encoded polypeptide. Such purification subsequences include, but are not limited to, metal chelating peptides such as histidine-tryptophan modules that allow purification on immobilized metals, a sequence which binds glutathione (e.g., GST), a hemagglutinin (HA) tag (corresponding to an epitope derived from the influenza hemagglutinin protein; Wilson, I. et al. (1984) Cell 37:767), maltose binding protein sequences, the FLAG epitope utilized in the FLAGS extension/affinity purification system, and the like. The inclusion of a protease-cleavable polypeptide linker sequence between the purification domain and the polypeptide sequence is useful to facilitate purification.

For example, one expression vector possible to use in the compositions and methods described herein provides for expression of a fusion protein comprising a polypeptide of the invention fused to a polyhistidine region separated by an enterokinase cleavage site. The histidine residues facilitate purification on IMIAC (immobilized metal ion affinity chromatography, as described in Porath et al. (1992) Protein Expression and Purification 3:263-281) while the enterokinase cleavage site provides a method for separating the desired polypeptide from the polyhistidine region. pGEX vectors (Promega; Madison, WI) are optionally used to express foreign polypeptides as fusion proteins with glutathione S-transferase (GST). In general, such fusion proteins are soluble and can easily be purified from lysed cells by adsorption to ligand-agarose beads (e.g., glutathione-agarose in the case of GST-fusions) followed by elution in the presence of free ligand.

An additional construction in the compositions and methods described herein provides for proteins, and their encoding nucleic acids, comprising polypeptides of the invention (or one or more fragments thereof), e.g., as described herein, fused to an Ig molecule, e.g., human IgG Fc ("fragment crystallizable," or fragment complement

binding) hinge, CH2 domain and CH3 domain (and nucleotide sequences encoding them). Fc is the portion of the antibody responsible for binding to antibody receptors on cells and the C1q component of complement. These fusion proteins or fragments thereof and their encoding nucleic acids are optionally useful as prophylactic and/or therapeutic drugs or as diagnostic tools (see also, e.g., Challita-Eid, P. et al. (1998) J Immunol 160:3419-3426; Sturmhoefel, K. et al. (1999) Cancer Res 59:4964-4972).

Polypeptide Production and Recovery

Following transduction of a suitable host strain and growth of the host strain to an appropriate cell density, the selected promoter is induced by appropriate means (e.g., temperature shift or chemical induction) and cells are cultured for an additional period. Cells are typically harvested by centrifugation, disrupted by physical or chemical means, and the resulting crude extract retained for further purification. Eukaryotic or microbial cells employed in expression of the proteins can be disrupted by any convenient method, including freeze-thaw cycling, sonication, mechanical disruption, or use of cell lysing agents, or other methods, which are well know to those skilled in the art.

As noted, many references are available for the culture and production of many cells, including cells of bacterial, plant, animal (especially mammalian) and archebacterial origin. See, e.g., Sambrook, Ausubel, and Berger (all *supra*), as well as Freshney (1994) Culture of Animal Cells, a Manual of Basic Technique, third edition, Wiley-Liss, New York and the references cited therein; Doyle and Griffiths (1997) Mammalian Cell Culture: Essential Techniques John Wiley and Sons, NY; Humason (1979) Animal Tissue Techniques, fourth edition W.H. Freeman and Company; and Ricciardelli et al. (1989) *In vitro* Cell Dev Biol 25:1016-1024. For plant cell culture and regeneration see, e.g., Payne et al. (1992) Plant Cell and Tissue Culture in Liquid Systems John Wiley & Sons, Inc. New York, NY; Gamborg and Phillips (eds.) (1995) Plant Cell, Tissue and Organ Culture; Fundamental Methods Springer Lab Manual, Springer-Verlag (Berlin Heidelberg New York) and Plant Molecular Biology (1993) R.R.D. Croy (ed.) Bios Scientific Publishers, Oxford, U.K. ISBN 0 12 198370 6. Cell culture media in general are set forth in Atlas and Parks (eds.) The Handbook of Microbiological Media (1993) CRC Press, Boca Raton, FL. Additional information for cell culture is found in available commercial literature such as the Life Science Research Cell Culture Catalogue from Sigma-Aldrich,

Inc (St Louis, MO) ("Sigma-LSRCCC") and, e.g., the Plant Culture Catalogue and supplement also from Sigma-Aldrich, Inc (St Louis, MO) ("Sigma-PCCS").

Polypeptides of the invention can be recovered and purified from recombinant cell cultures by any of a number of methods well known in the art, including ammonium sulfate or ethanol precipitation, acid extraction, anion or cation exchange chromatography, phosphocellulose chromatography, hydrophobic interaction chromatography, affinity chromatography (e.g., using any of the tagging systems noted herein), hydroxylapatite chromatography, and lectin chromatography. Protein refolding steps can be used, as desired, in completing configuration of the mature protein or fragments thereof. Finally, high performance liquid chromatography (HPLC) can be employed in the final purification steps. In addition to the references noted, *supra*, a variety of purification methods are well known in the art, including, e.g., those set forth in Sandana (1997) Bioseparation of Proteins, Academic Press, Inc.; Bollag et al. (1996) Protein Methods, 2nd Edition Wiley-Liss, NY; Walker (1996) The Protein Protocols Handbook Humana Press, NJ; Harris and Angal (1990) Protein Purification Applications: A Practical Approach IRL Press at Oxford, Oxford, England; Harris and Angal Protein Purification Methods: A Practical Approach IRL Press at Oxford, Oxford, England; Scopes (1993) Protein Purification: Principles and Practice 3rd Edition Springer Verlag, NY; Janson and Ryden (1998) Protein Purification: Principles, High Resolution Methods and Applications, Second Edition Wiley-VCH, NY; and Walker (1998) Protein Protocols on CD-ROM Humana Press, NJ.

In vitro Expression Systems

Cell-free transcription/translation systems can also be employed to produce polypeptides of the invention using polynucleotides of the present invention. Several such systems are commercially available. A general guide to *in vitro* transcription and translation protocols is found in Tymms (1995) *In vitro* Transcription and Translation Protocols: Methods in Molecular Biology Volume 37, Garland Publishing, NY.

In vivo Uses and Applications

Polynucleotides that encode a polypeptide of the invention, or complements of the polynucleotides (including e.g., antisense or ribozyme molecules), are optionally

administered to a cell to accomplish a therapeutically useful process or to express a therapeutically useful product. These *in vivo* applications, including gene therapy, include a multitude of techniques by which gene expression may be altered in cells. Such methods include, for instance, the introduction of genes for expression of, e.g., therapeutically and/or prophylactically useful polypeptides, such as the polypeptides of the present invention.

In vivo Polypeptide Expression

Polynucleotides encoding polypeptides of the invention are particularly useful for *in vivo* therapeutic applications, using techniques well known to those skilled in the art. For example, cultured cells are engineered *ex vivo* with at least one polynucleotide (DNA or RNA) of the invention and/or other polynucleotide sequences encoding, e.g., at least one of an antigen, cytokine, other co-stimulatory molecule, adjuvant, etc., and the like, with the engineered cells then being returned to the patient. Cells may also be engineered *in vivo* for expression of one or more polypeptides *in vivo*, including polypeptides and/or antigenic peptides of the invention.

A number of viral vectors suitable for organismal *in vivo* transduction and expression are known. Such vectors include retroviral vectors (see, e.g., Miller, Curr Top Microbiol Immunol (1992) 158:1-24; Salmons and Gunzburg (1993) Human Gene Therapy 4:129-141; Miller et al. (1994) Methods in Enzymology 217:581-599) and adeno-associated vectors (reviewed in Carter (1992) Curr Opinion Biotech 3:533-539; Muzcyzka (1992) Curr Top Microbiol Immunol. 158:97-129). Other viral vectors that are used include adenoviral vectors, herpes viral vectors and Sindbis viral vectors, as generally described in, e.g., Jolly (1994) Cancer Gene Therapy 1:51-64; Latchman (1994) Molec Biotechnol 2:179-195; and Johanning et al. (1995) Nucl Acids Res 23:1495-1501.

In one aspect, a pox virus vector can be used. The pox viral vector is transfected with a polynucleotide sequence encoding a polypeptide of the invention, such as an eIL-2 polypeptide, and is useful in prophylactic, therapeutic and diagnostic applications where enhancement of an immune response, such as e.g., increased or improved T cell proliferation is desired. See viral vectors discussed in, e.g., Berencsi et al., J Infect Dis (2001)183(8):1171-9; Rosenwirth et al., Vaccine 2001 Feb 8;19(13-14):1661-70; Kittlesen et al., J Immunol (2000) 164(8):4204-11; Brown et al. Gene Ther 2000

7(19):1680-9; Kanesa-thasan et al., Vaccine (2000) 19(4-5):483-91; Sten (2000) Drug 60(2):249-71. Compositions comprising such vectors and an acceptable excipient are also a feature of the invention.

Gene therapy and genetic vaccines provide methods for combating chronic infectious diseases (e.g., HIV infection, viral hepatitis), as well as non-infectious diseases including cancer and some forms of congenital defects such as enzyme deficiencies, and such methods can be employed with polynucleotides of the invention, including, e.g., vectors and cells comprising such polynucleotides. Several approaches for introducing nucleic acids and vectors into cells *in vivo*, *ex vivo* and *in vitro* have been used and can be employed with polynucleotides of the invention, and vectors comprising such polynucleotides. These approaches include liposome based gene delivery (Debs and Zhu (1993) WO 93/24640 and U.S. Pat. No. 5,641,662; Mannino and Gould-Fogerite (1988) BioTechniques 6(7):682-691; Rose, U.S. Pat. No. 5,279,833; Brigham (1991) WO 91/06309; and Felgner et al. (1987) Proc Natl Acad Sci USA 84:7413-7414; Brigham et al. (1989) Am J Med Sci 298:278-281; Nabel et al. (1990) Science 249:1285-1288; Hazinski et al. (1991) Am J Resp Cell Molec Biol 4:206-209; and Wang and Huang (1987) Proc Natl Acad Sci USA 84:7851-7855); adenoviral vector mediated gene delivery, e.g., to treat cancer (see, e.g., Chen et al. (1994) Proc Natl Acad Sci USA 91:3054-3057; Tong et al. (1996) Gynecol Oncol 61:175-179; Clayman et al. (1995) Cancer Res. 5:1-6; O'Malley et al. (1995) Cancer Res 55:1080-1085; Hwang et al. (1995) Am J Respir Cell Mol Biol 13:7-16; Haddada et al. (1995) Curr Top Microbiol Immunol. 1995 (Pt. 3):297-306; Addison et al. (1995) Proc Natl Acad Sci USA 92:8522-8526; Colak et al. (1995) Brain Res 691:76-82; Crystal (1995) Science 270:404-410; Elshami et al. (1996) Human Gene Ther 7:141-148; Vincent et al. (1996) J Neurosurg 85:648-654), and many others. Replication-defective retroviral vectors harboring therapeutic polynucleotide sequence as part of the retroviral genome have also been used, particularly with regard to simple MuLV vectors. See, e.g., Miller et al. (1990) Mol Cell Biol 10:4239 (1990); Kolberg (1992) J NIH Res 4:43, and Cornetta et al. (1991) Hum Gene Ther 2:215). Nucleic acid transport coupled to ligand-specific, cation-based transport systems (Wu and Wu (1988) J Biol Chem, 263:14621-14624) has also been used. Naked DNA expression vectors have also been described (Nabel et al. (1990), *supra*); Wolff et al. (1990) Science, 247:1465-1468). In general, these approaches can be adapted to the

invention by incorporating nucleic acids encoding the polypeptides of the invention into the appropriate vectors.

General texts which describe gene therapy protocols, which can be adapted to the present invention by introducing the nucleic acids of the invention into patients, include, e.g., Robbins (1996) Gene Therapy Protocols, Humana Press, NJ, and Joyner (1993) Gene Targeting: A Practical Approach, IRL Press, Oxford, England.

Antisense Technology

In addition to expression of the nucleic acids of the invention as gene replacement nucleic acids, the nucleic acids are also useful for sense and anti-sense suppression of expression, e.g., to down-regulate expression of a nucleic acid of the invention, once, or when, expression of the nucleic acid is no-longer desired in the cell. Similarly, the nucleic acids of the invention, or subsequences or anti-sense sequences thereof, can also be used to block expression of naturally occurring homologous nucleic acids. A variety of sense and anti-sense technologies are known in the art, e.g., as set forth in Lichtenstein and Nellen (1997) Antisense Technology: A Practical Approach IRL Press at Oxford University, Oxford, England, and in Agrawal (1996) Antisense Therapeutics Humana Press, NJ, and the references cited therein.

Use as Probes

Also contemplated are uses of polynucleotides, also referred to herein as oligonucleotides, typically having at least 12 bases, preferably at least 15, more preferably at least 20, at least 30, or at least 50 or more bases, which hybridize under highly stringent conditions to a polynucleotide of the invention, or fragments thereof. The polynucleotides may be used as probes, primers, sense and antisense agents, and the like, according to methods as noted *supra*.

THERAPEUTIC USES

Various interferon-alpha polypeptides and interferon-alpha conjugates have been approved or are currently in clinical development for treatment of a variety of conditions such as Chronic Hepatitis C, Chronic Hepatitis B, Hairy Cell Leukemia, Malignant Melanoma, Follicular Lymphoma, Condylomata Acuminata, AIDS-related Kaposi's

Sarcoma, Non-Hodgkin's Lymphoma, Chronic Melogenous Leukemia, Basal Cell Carcinoma, Multiple Myeloma, carcinoid tumors, bladder cancer, Crohn's Disease, Cutaneous T Cell Lymphoma, Renal Cell Carcinoma, Multiple Sclerosis, and AIDS. Accordingly, the present invention includes a method of treating a condition which is responsive to interferon-alpha, such as for example a condition described above, comprising administering to a subject afflicted with the condition a composition comprising a polypeptide of the invention or a conjugate of the invention in an amount effective to ameliorate a symptom associated with the condition. The invention also includes the use of a composition comprising a polypeptide of the invention or a conjugate of the invention (i.e., a "composition of the invention") to treat a condition which is responsive to interferon-alpha, such as a condition described above, or any other condition which is responsive to a polypeptide of the invention or a conjugate of the invention.

Treatment of Viral Infections and Conditions Associated with Viral Infection

In one aspect, the invention provides a method for treating a subject infected with a virus, comprising administering to the subject a composition of the invention in an amount effective to decrease the level of the virus in the subject and/or to ameliorate a symptom or condition associated with the viral infection. Exemplary viral infections contemplated for treatment methods of the invention include, but are not limited to, infection by a virus of the *Flaviviridae* family, such as, for example, Hepatitis C Virus, Yellow Fever Virus, West Nile Virus, Japanese Encephalitis Virus, Dengue Virus, or Bovine Viral Diarrhea Virus; infection by a virus of the *Hepadnaviridae* family, such as, for example, Hepatitis B Virus; infection by a virus of the *Picornaviridae* family, such as, for example, Encephalomyocarditis Virus, Human Rhinovirus, or Hepatitis A Virus; infection by a virus of the *Retroviridae* family, such as, for example, Human Immunodeficiency Virus, Simian Immunodeficiency Virus, Human T-Lymphotropic Virus, or Rous Sarcoma Virus; infection by a virus of the *Coronaviridae* family, such as, for example, SARS coronavirus; infection by a virus of the *Rhabdoviridae* family, such as, for example, Rabies Virus or Vesicular Stomatitis Virus, infection by a virus of the *Paramyxoviridae* family, such as, for example, Respiratory Syncytial Virus or Parainfluenza Virus, infection by a virus of the *Papillomaviridae* family, such as, for

example, Human Papillomavirus, and infection by a virus of the *Herpesviridae* family, such as, for example, Herpes Simplex Virus.

The following provides non-limiting examples for treatment of exemplary viral infections and diseases and conditions associated with such infections using polypeptides and conjugates of the invention, including suggested dosing schedules for polypeptides and conjugates of the invention and approaches to monitoring the efficacy of such treatments. The dosing schedules of polypeptides or conjugates of the invention for the treatment of other viral infections and diseases and conditions associated with viral infections, and approaches to monitoring the efficacy of such treatments, is ascertainable by one skilled in the art.

Hepatitis C Virus

In one aspect the invention provides a method of treating a patient infected with Hepatitis C Virus (HCV), comprising administering to the patient an effective amount of a composition of the invention comprising one or more polypeptide or conjugate of the invention. The invention also provides a composition for use in treating a patient infected with HCV, comprising one or more polypeptide or conjugate of the invention and a pharmaceutically acceptable carrier or excipient. A patient diagnosed as infected with HCV includes a patient exhibiting HCV RNA in the blood and/or exhibiting anti-HCV antibody in the serum.

A composition comprising a polypeptide of the invention will generally be administered at a dose and frequency similar to what is employed in HCV therapeutic regimens using clinically-approved interferon-alpha polypeptides, such as, e.g. ROFERON®-A (Interferon alfa-2a, recombinant; Hoffmann-La Roche Inc.), INTRON® A (Interferon alfa-2b, recombinant; Schering Corporation), and INFERGEN® (interferon alfacon-1; InterMune, Inc.). Exemplary recommended dosing schedules of ROFERON or INTRON A for the treatment of chronic HCV is 3 million IU (approximately 15 micrograms (mcg)) three times a week by subcutaneous injection for, e.g., 24 to 48 weeks. An exemplary recommended dosing schedule of INFERGEN for the treatment of chronic HCV is 9 mcg three times a week by subcutaneous injection for, e.g., 24 to 48 weeks. Depending on a number of factors (including but not limited to the activity and the pharmacokinetics of the polypeptide of the invention and the size and health of the

patient), the polypeptide may be administered in lower amounts (such as, for example, about 2, 3, 4, 5, 6, 7, or 8 mcg) and/or less frequently (such as once per week or twice per week) than described above.

Likewise, a composition comprising a conjugate of the invention will generally be administered at a dose and frequency similar to what is employed in HCV therapeutic regimens using clinically-approved interferon-alpha conjugates, such as, e.g., PEGASYS® (Peginterferon alfa-2a; Hoffmann-La Roche, Inc.) or PEG-INTRON® (peginterferon alfa-2b; Schering Corporation). An exemplary recommended dosing schedule of PEGASYS for the treatment of chronic HCV is 180 mcg once weekly by subcutaneous injection for, e.g., 24 to 48 weeks. Depending on a number of factors (including but not limited to the molecular weight, activity, and pharmacokinetics of the conjugate of the invention and the size and health of the patient), the conjugate may be administered in lower amounts (such as, for example, about 25, 50, 75, 100, 125, or 150 mcg) and/or less frequently (such as once every 10 days, or once every 2 weeks) than described above.

In some instances the polypeptide or conjugate of the invention is administered in combination with one or more additional therapeutic agent(s). For example, the polypeptide or conjugate of the invention may be administered in combination with a small-molecule antiviral drug such as Ribavirin, which is sold under the names COPEGUS® (Hoffmann-La Roche, Inc) and REBETOL® (Schering Corporation). Alternatively, or in addition to a small-molecule antiviral drug, the polypeptide or conjugate of the invention may be administered in combination with one or more additional cytokine, such as, for example, IFN-gamma, which is sold under the name Actimmune® (interferon gamma-1b; InterMune, Inc.), IL-2, which is sold under the name PROLEUKIN® IL-2 (aldesleukin recombinant human interleukin-2 (rhIL-2); Chiron Corp.), or IL-12 (interleukin-12).

The precise amount and frequency of administration of the polypeptide or conjugate of the invention will depend on a number of factors such as the specific activity and the pharmacokinetic properties of the polypeptide or the conjugate, as well as the nature of the condition being treated (such as, the genotype of the Hepatitis C virus being treated), among other factors known to those of skill in the art. Normally, the dose should be capable of preventing or lessening the severity or spread of the indication being treated.

Such a dose may be termed an "effective" or "therapeutically effective" amount. It will be apparent to those of skill in the art that an effective amount of a polypeptide, conjugate or composition of the invention depends, *inter alia*, upon the condition being treated, the dose, the administration schedule, whether the polypeptide or conjugate or composition is administered alone or in combination with other therapeutic agents, the serum half-life and other pharmacokinetic properties of the polypeptide, conjugate or composition, as well as the size, age, and general health of the patient. The dosage and frequency of administration is ascertainable by one skilled in the art using known techniques.

The effectiveness of treatment may be determined by measuring viral load, for example by determining the titer or level of virus in serum or plasma using methods known in the art, such as, e.g., by monitoring viral RNA levels using quantitative PCR-based tests, such as the COBAS AMPLICOR® HCV Test, v2.0 or the COBAS AMPLICOR HCV MONITOR® Test, v2.0 (both from Roche Diagnostics). In some instances, an effective amount of a composition of the invention is one that is sufficient to achieve a reduction in viral load by at least 2 log units, at least 3 log units, at least 4 log units, at least 5 log units, at least 6 log units or at least 7 log units over the course of treatment, compared to the viral load prior to treatment (which is generally in the range of 10^5-10^7 copies of HCV RNA/ml for chronic HCV patients). In some instances an effective amount of a composition of the invention is an amount that is sufficient to reduce viral load to levels which are essentially undetectable, such as, for example, less than about 500 copies/ml serum or less than about 100 copies/ml serum. The invention includes a method of reducing the level of HCV RNA in serum of a patient infected with HCV, comprising administering to the patient a composition of the invention in an amount effective to reduce the level of HCV RNA compared to the HCV RNA level present prior to the start of treatment.

The effectiveness of treatment may alternatively or in addition be determined by measuring a parameter indicative of a condition associated with HCV infection, such as, e.g., liver damage. For example, the level of serum alanine aminotransferase (ALT) may be measured using a standard assay. In general, an ALT level of less than about 50 international units/ml (IU/ml) serum is considered normal. A higher ALT level may be indicative of ongoing liver damage. In some instances, an effective amount of a composition of the invention is an amount effective to reduce ALT level, in a patient with

a higher than normal ALT level, to less than about 50 IU/ml of serum. Thus, the invention includes a method of reducing the serum ALT level of a patient infected with HCV exhibiting an initial ALT level greater than 50 IU/ml, comprising administering to the patient a composition of the invention in an amount effective to reduce the ALT level to less than about 50 IU/ml.

Human Immunodeficiency Virus

In another aspect the invention provides a method of treating a patient infected with Human Immunodeficiency Virus (HIV), such as HIV-1 or HIV-2, or a disease or condition associated with HIV infection, such as, for example, AIDS-related Kaposi's sarcoma, comprising administering to the patient an effective amount of a composition of the invention comprising one or more polypeptide or conjugate of the invention, optionally in association with other antiviral therapeutic agents as described below. The invention also provides a composition for use in treating a patient infected with HIV or a disease or condition associated with HIV infection, comprising one or more polypeptide or conjugate of the invention and a pharmaceutically acceptable carrier or excipient. A patient diagnosed as infected with HIV includes a patient exhibiting detectable levels of HIV RNA or proviral DNA in the blood, and/or exhibiting detectable levels of p24 antigen or anti-HIV antibody in serum.

A composition comprising a polypeptide of the invention will generally be administered at a dose and frequency similar to what is employed in HIV therapeutic regimens using interferon-alpha polypeptides such as, e.g. ROFERON®-A (Interferon alfa-2a, recombinant; Hoffmann-La Roche Inc.), INTRON® A (Interferon alfa-2b, recombinant; Schering Corporation), and INFERGEN® (interferon alfacon-1; InterMune, Inc.). As was noted above, exemplary recommended dosing schedules of ROFERON or INTRON A for the treatment of chronic HCV is 3 million IU (approximately 15 micrograms (mcg)) three times a week by subcutaneous injection for, e.g., 24 to 48 weeks, and a exemplary recommended dosing schedule of INFERGEN for the treatment of chronic HCV is 9 mcg three times a week by subcutaneous injection for, e.g., 24 to 48 weeks. An exemplary recommended dosing schedule of ROFERON for the treatment of AIDS-related Kaposi's sarcoma is 36 million units daily for 10 to 12 weeks, then 36 million units 3 times a week. An exemplary recommended dosing schedule of INTRON

A for the treatment of AIDS-related Kaposi's sarcoma is 30 million IU/m2 three times a week administered subcutaneously. Such dosing schedules provide useful ranges for dosage of a polypeptide of the invention for the treatment of HIV or a disease or condition associated with HIV infection. Depending on a number of factors (including but not limited to the activity and the pharmacokinetics of the polypeptide of the invention and the size, age and health of the patient), the polypeptide of the invention may be administered in lower amounts and/or less frequently than described above.

Likewise, a composition comprising a conjugate of the invention will generally be administered at a dose and frequency similar to what is employed in HIV therapeutic regimens using interferon-alpha conjugates, such as, e.g., PEGASYS® (Peginterferon alfa-2a; Hoffmann-La Roche, Inc.) or PEG-INTRON® (peginterferon alfa-2b; Schering Corporation). An exemplary dosing schedule of PEG-INTRON for the treatment of HIV is between about 1.0 mcg/kg/week and 3.0 mcg/kg/week by subcutaneous injection for, e.g., 24 to 48 weeks. Such a dosing schedule provides a useful range for dosage of a conjugate of the invention for the treatment of HIV. Depending on a number of factors (including but not limited to the molecular weight, activity, and pharmacokinetics of the conjugate of the invention and the size, age and health of the patient), the conjugate may be administered in lower amounts (such as, for example, about 0.1, 0.25, 0.50, or 0.75 mcg/kg/week) and/or less frequently (such as once every 10 days, or once every 2 weeks) than described above.

In some instances the polypeptide or conjugate of the invention is administered in combination with one or more additional therapeutic agent(s). Current clinical treatments of HIV-1 infection in man include multi-drug combination therapies generally termed Highly Active Antiretroviral Therapy ("HAART"). The polypeptide or conjugate of the invention may thus be administered in combination with HAART or other antiviral therapeutic compounds. Typical components of HAART, which involve various combinations of nucleoside reverse transcriptase inhibitors ("NRTI"), non-nucleoside reverse transcriptase inhibitors ("NNRTI") and HIV protease inhibitors ("PI"), are described, for example, in A.M. Vandamme *et al.* (1998) Antiviral Chemistry & Chemotherapy, 9:187-203; "Drugs for HIV Infection" in The Medical Letter Vol. 39 (Issue 1015) December 5, 1997, pages 111-116; and published United States Patent Application US 20020182179 A1; each of which is incorporated by reference herein. If

the HIV-infected patient is also infected with HCV, the polypeptide or conjugate of the invention may be administered in combination with an antiviral drug such as Ribavirin, which is sold under the names COPEGUS® (Hoffmann-La Roche, Inc) and REBETOL® (Schering Corporation), along with HAART.

The precise amount and frequency of administration of the polypeptide or conjugate of the invention, and administration of additional therapeutic agents such as HAART and/or Ribavirin, will depend on a number of factors such as the specific activity and the pharmacokinetic properties of the polypeptide or the conjugate, as well as the nature of the condition being treated (such as, the presence of additional viral infections such as HCV), among other factors known to those of skill in the art. Normally, the dose should be capable of preventing or lessening the severity or spread of the indication being treated. Such a dose may be termed an "effective" or "therapeutically effective" amount. It will be apparent to those of skill in the art that an effective amount of a polypeptide, conjugate or composition of the invention depends, *inter alia*, upon the condition being treated, the dose, the administration schedule, whether the polypeptide or conjugate or composition is administered alone or in combination with other therapeutic agents, the serum half-life and other pharmacokinetic properties of the polypeptide, conjugate or composition, as well as the size, age, and general health of the patient. The dosage and frequency of administration is ascertainable by one skilled in the art using known techniques.

In addition to general uses described above, a polypeptide or conjugate of the invention may be administered to the following subsets of patients infected with HIV: as an adjuvant therapy, for example to HAART as described above; as monotherapy or combination therapy in early stage patients when the viral load is generally high; as a combined anti-viral and immunodulatory agent for patients undergoing structured treatment interruptions (STI) or "drug holidays"; as salvage therapy in patients whose HAART options are limited; as an antiviral method of treatment to keep viral load in check without initiating HAART therapy in order to delay the appearance of HAART resistant virus.

The effectiveness of treatment may be determined by measuring viral load, for example by determining the titer or level of virus in serum or plasma using methods known in the art, such as, e.g., by monitoring HIV-1 viral RNA levels using quantitative

RT-PCR based tests, such as the AMPLICOR HIV-1 MONITOR® Test, v1.5 (Roche Diagnostics). In some instances, an effective amount of a composition of the invention is one that is sufficient to achieve a reduction in viral load by at least 0.5 log units, at least 1 log unit, at least 2 log units, at least 3 log units, at least 4 log units, at least 5 log units, at least 6 log units or at least 7 log units over the course of treatment, compared to the viral load prior to treatment. In some instances an effective amount of a composition of the invention is an amount that is sufficient to reduce viral load to levels which are essentially undetectable, such as, for example, less than about 50-100 copies HIV-1 RNA per ml serum. The invention includes a method of reducing the level of HIV RNA in serum of a patient infected with HIV, comprising administering to the patient a composition of the invention in an amount effective to reduce the level of HIV RNA compared to the HIV RNA level present prior to the start of treatment.

The effectiveness of treatment may alternatively or in addition be determined by a serum markers for HIV replication, such as the presence of HIV p24 antigen in the blood. In some instances an effective amount of a composition of the invention is an amount that is sufficient to reduce the level of p24 antigen in the blood to 50%, 25%, 10% or 5% of the level present prior to the start of treatment. In some instances an effective amount of a composition of the invention is an amount that is sufficient to reduce the level of p24 antigen to a level which is essentially undetectable. The invention includes a method of reducing the level of p24 antigen in serum of a patient infected with HIV, comprising administering to the patient a composition of the invention in an amount effective to reduce the level of p24 antigen compared to the p24 antigen level present prior to the start of treatment.

Hepatitis B Virus

In another aspect, the invention provides a method of treating a patient infected with Hepatitis B Virus (HBV), comprising administering to the patient an effective amount of a composition of the invention comprising one or more polypeptide or conjugate of the invention. The invention also provides a composition for use in treating a patient infected with HBV, comprising one or more polypeptide or conjugate of the invention and a pharmaceutically acceptable carrier or excipient.

A patient diagnosed as infected with HBV exhibits detectable hepatitis B surface antigen (HBsAg) in the serum. Chronic HBV infection is further categorized as either "replicative" or "non-replicative". In replicative infection, the patient usually has a relatively high serum concentration of viral DNA and detectable HBeAg, which is an alternatively processed protein of the HBV pre-core gene that is synthesized under conditions of high viral replication. However, in rare strains of HBV with mutations in the pre-core gene, replicative infection can occur in the absence of detectable serum HBeAg. Patients with chronic hepatitis B and replicative infection have a generally worse prognosis and a greater chance of developing cirrhosis and/or hepatocellular carcinoma than those without HBeAg. In non-replicative infection, the rate of viral replication in the liver is low, serum HBV DNA concentration is generally low and hepatitis Be antigen (HBeAg) is not detected.

A composition comprising a polypeptide of the invention will generally be administered at a dose and frequency similar to what is employed in HBV therapeutic regimens using clinically-approved interferon-alpha polypeptides, such as, e.g. INTRON® A (Interferon alfa-2b, recombinant; Schering Corporation). An exemplary recommended dosing schedule of INTRON A for the treatment of chronic HBV in adults is 30 to 35 million IU per week by subcutaneous or intramuscular injection, either as 5 million IU per day (qd) or as 10 million IU three times per week (tiw) for 16 weeks. Depending on a number of factors (including, but not limited to, the activity and the pharmacokinetics of the polypeptide of the invention, and the size and health of the patient), the polypeptide of the invention may be administered in lower amounts (such as, for example, about 5, 10, 15, 20, or 25 million IU per week) and/or less frequently (such as once per week or twice per week) than described above.

Likewise, a composition comprising a conjugate of the invention will generally be administered at a dose and frequency similar to what is employed in HBV therapeutic regimens using interferon-alpha conjugates currently undergoing clinical trials, such as, e.g., PEGASYS® (Peginterferon alfa-2a; Hoffmann-La Roche, Inc.). Exemplary dosing schedules of PEGASYS for the treatment of chronic HBV is between 90 mcg-270 mcg injected once per week for a total of 24 weeks. Depending on a number of factors (including but not limited to the molecular weight, activity, and pharmacokinetics of the conjugate of the invention and the size and health of the patient), the conjugate may be

administered in lower amounts (such as, for example, about 25, 50, 75, 100, 125, 150, or 200 mcg) and/or less frequently (such as once every 10 days, or once every 2 weeks) than described above.

In some instances the polypeptide or conjugate of the invention is administered in combination with one or more additional therapeutic agent(s). For example, the polypeptide or conjugate of the invention may be administered in combination with antiviral drugs such as lamivudine (also known as 3TC), which is sold under the name Epivir-HBV® (GlaxoSmithKline), or adefovir dipivoxil, which is sold under the name Hepsera® (Gilead Sciences).

The precise amount and frequency of administration of the polypeptide or conjugate of the invention will depend on a number of factors such as the specific activity and the pharmacokinetic properties of the polypeptide or the conjugate, as well as the nature of the condition being treated (such as, e.g., in the case of chronic HBV infection, whether the infection is replicative or non-replicative), among other factors known to those of skill in the art. Normally, the dose should be capable of preventing or lessening the severity or spread of the indication being treated. Such a dose may be termed an "effective" or "therapeutically effective" amount. It will be apparent to those of skill in the art that an effective amount of a polypeptide, conjugate or composition of the invention depends, *inter alia*, upon the condition being treated, the dose, the administration schedule, whether the polypeptide or conjugate or composition is administered alone or in combination with other therapeutic agents, the serum half-life and other pharmacokinetic properties of the polypeptide, conjugate or composition, as well as the size, age, and general health of the patient. The dosage and frequency of administration is ascertainable by one skilled in the art using known techniques.

The effectiveness of treatment may be determined for example by measuring the viral load, e.g. the level of viral DNA in serum or plasma, using methods known in the art. Methods for monitoring HBV DNA levels include quantitative PCR-based tests, such as the COBAS AMPLICOR HBV MONITOR® Test, v2.0 or the AMPLICOR HBV MONITOR® Test, v2.0 (both from Roche Diagnostics). In some instances an effective amount of a composition of the invention is an amount that is sufficient to reduce viral DNA to, e.g., less than about 500,000 copies/ml serum or less than about 100,000 copies/ml serum or less than about 10,000 copies/ml serum, or to levels which are

essentially undetectable (such as, for example, less than about 1000 copies/ml serum, less than about 500 copies/ml serum, or less than about 200 copies/ml serum). The invention includes a method of reducing the level of HBV DNA in serum of a patient infected with HBV, comprising administering to the patient a composition of the invention in an amount effective to reduce the level of HBV DNA compared to the HBV DNA level present prior to the start of treatment.

The effectiveness of treatment may alternatively or in addition be determined by measuring other serum markers for HBV replication, such as HBeAg. In some instances an effective amount of a composition of the invention is an amount that is sufficient to reduce the level of HBeAg in serum to 50%, 25%, 10% or 5% of the level present prior to the start of treatment. In some instances an effective amount of a composition of the invention is an amount that is sufficient to reduce the level of HBeAg to a level which is essentially undetectable. The invention includes a method of reducing the level of HBeAg in serum of a patient infected with HBV, comprising administering to the patient a composition of the invention in an amount effective to reduce the level of HBeAg compared to the HBeAg level present prior to the start of treatment.

As discussed above, another serum marker indicative of HBV infection is HBsAg. Thus, the effectiveness of treatment may alternatively or in addition be determined by measuring the level of HBsAg in the serum. In some instances an effective amount of a composition of the invention is an amount that is sufficient to reduce the level of HBsAg in serum to 50%, 25%, 10% or 5% of the level present prior to the start of treatment. In some instances an effective amount of a composition of the invention is an amount that is sufficient to reduce level of HBsAg to a level which is essentially undetectable. The invention includes a method of reducing the level of HBsAg in serum of a patient infected with HBV, comprising administering to the patient a composition of the invention in an amount effective to reduce the level of HBsAg compared to the HBsAg level present prior to the start of treatment.

The effectiveness of treatment may alternatively or in addition be determined by measuring a parameter indicative of a condition associated with HBV infection, such as, e.g., liver damage. For example, the level of serum alanine aminotransferase (ALT) may be measured using a standard assay. In general, an ALT level of less than about 50 international units/ml (IU/ml) serum is considered normal. A higher ALT level may be

indicative of ongoing liver damage. In some instances, an effective amount of a composition of the invention is an amount effective to reduce ALT level, in a patient with a higher than normal ALT level, to less than about 50 IU/ml of serum. Thus, the invention includes a method of reducing the serum ALT level of a patient infected with HBV exhibiting an initial ALT level greater than 50 IU/ml, comprising administering to the patient a composition of the invention in an amount effective to reduce the ALT level to less than about 50 IU/ml.

Human T-Lymphotropic Virus type 1

In another aspect the invention provides a method of treating a patient infected with Human T-Lymphotropic Virus type 1 (HTLV-1), or a disease or condition associated with HTLV-1 infection, such as, for example, adult T-cell leukemia/lymphoma (ATLL), HTLV-1-associated myelopathy (HAM), Tropical Spastic Paraparesis (TSP), uveitis, or arthropathy. The method comprises administering to the patient an effective amount of a composition of the invention comprising one or more polypeptide or conjugate of the invention. The invention also provides a composition for use in treating a patient infected with HTLV-1, or a disease or condition associated with HTLV-1 infection, the composition comprising one or more polypeptide or conjugate of the invention and a pharmaceutically acceptable carrier or excipient. A patient diagnosed with HTLV-1 infection includes a patient exhibiting HTLV-1 proviral DNA in the blood and/or antibody to an HTLV-1 antigen in the serum.

A composition comprising a polypeptide of the invention will generally be administered at a dose and frequency similar to what is employed in HCV or oncology therapeutic regimens using clinically-approved interferon-alpha polypeptides, such as, e.g. ROFERON®-A (Interferon alfa-2a, recombinant; Hoffmann-La Roche Inc.) and INTRON® A (Interferon alfa-2b, recombinant; Schering Corporation). Exemplary recommended dosing schedules of ROFERON or INTRON A for the treatment of chronic HCV is 3 million IU (approximately 15 micrograms (mcg)) three times a week by subcutaneous injection for, e.g., 24 to 48 weeks. An exemplary recommended dosing schedule of ROFERON for the treatment of hairy-cell leukemia is 3-5 million units daily by subcutaneous injection for 16 to 24 weeks, then 3 million units 3 times a week for maintenance. An exemplary recommended dosing schedule of INTRON A for the

treatment of hairy-cell leukemia is 2 million IU/m2 (square meter of body surface) administered subcutaneously 3 times a week for 6 months. Such dosing schedules provide useful ranges for dosage of a polypeptide of the invention for the treatment of HTLV-1 infection, or a disease or condition associated with HTLV-1 infection such as adult T-cell leukemia/lymphoma (ATLL), HTLV-1-associated myelopathy (HAM), or Tropical Spastic Paraparesis (TSP). Depending on a number of factors (including but not limited to the activity and the pharmacokinetics of the polypeptide of the invention and the size, age and health of the patient), the polypeptide may be administered in lower amounts and/or less frequently than described above.

Likewise, a composition comprising a conjugate of the invention will generally be administered at a dose and frequency similar to what is employed in HCV therapeutic or oncology therapeutic regimens using clinically-approved interferon-alpha conjugates, such as, e.g., PEGASYS® (Peginterferon alfa-2a; Hoffmann-La Roche, Inc.) or PEG-INTRON® (peginterferon alfa-2b; Schering Corporation). An exemplary recommended dosing schedule of PEGASYS for the treatment of chronic HCV is 180 mcg once weekly by subcutaneous injection for, e.g., 24 to 48 weeks. An exemplary recommended dosing schedule of PEG-INTRON for the treatment of chronic myelogenous leukemia is 6 mcg /kg body weight once weekly by subcutaneous injection for, e.g., 52 weeks. Such dosing schedules provide useful ranges for dosage of a conjugate of the invention for the treatment of HTLV-1 infection, or a disease or condition associated with HTLV-1 infection such as adult T-cell leukemia/lymphoma (ATLL), HTLV-1-associated myelopathy (HAM), or Tropical Spastic Paraparesis (TSP). Depending on a number of factors (including but not limited to the molecular weight, activity, and pharmacokinetics of the conjugate of the invention and the size, age and health of the patient), the conjugate may be administered in lower amounts and/or less frequently than described above.

In some instances the polypeptide or conjugate of the invention is administered in combination with one or more additional therapeutic agent(s). For example, the polypeptide or conjugate of the invention may be administered in combination with an antiretroviral drug such as zidovudine (AZT) and/or lamivudine (3TC). It may also be administered in combination with peripheral blood stem cell transplantation, conventional chemotherapy, or high dose chemotherapy with autologous or allogeneic bone marrow transplantation. Alternatively, the polypeptide or conjugate of the invention may be

combined with other immunotherapy, for example with anti-interleukin-2 receptor monoclonal antibodies or injection of cytotoxic T-cells directed against virus antigens.

The precise amount and frequency of administration of the polypeptide or conjugate of the invention will depend on a number of factors such as the specific activity and the pharmacokinetic properties of the polypeptide or the conjugate, as well as the nature of the condition being treated, among other factors known to those of skill in the art. Normally, the dose should be capable of preventing or lessening the severity or spread of the indication being treated. Such a dose may be termed an "effective" or "therapeutically effective" amount. It will be apparent to those of skill in the art that an effective amount of a polypeptide, conjugate or composition of the invention depends, *inter alia*, upon the condition being treated, the dose, the administration schedule, whether the polypeptide or conjugate or composition is administered alone or in combination with other therapeutic agents, the serum half-life and other pharmacokinetic properties of the polypeptide, conjugate or composition, as well as the size, age, and general health of the patient. The dosage and frequency of administration is ascertainable by one skilled in the art using known techniques.

The effectiveness of treatment may be determined by measuring the HTLV-1 viral load, such as, for example, measuring the level of HTLV-1 proviral DNA in the blood using methods known in the art, for example by quantitative PCR as described by Saito *et al.*, (2004) J. Infect Dis. 189(1):29-40. In some instances, an effective amount of a composition of the invention is one that is sufficient to achieve a reduction in viral load by at least 0.5 log unit, such as at least 1 log unit, at least 2 log units, at least 3 log units, at least 4 log units, at least 5 log units, at least 6 log units, or at least 7 log units over the course of treatment, compared to the viral load prior to treatment. In some instances an effective amount of a composition of the invention is an amount that is sufficient to reduce viral load to levels which are essentially undetectable. The invention includes a method of reducing the level of HTLV-1 proviral DNA in blood of a patient infected with HTLV-1, comprising administering to the patient a composition of the invention in an amount effective to reduce the level of HTLV-1 proviral DNA compared to that present prior to the start of treatment.

The effectiveness of treatment may alternatively or in addition be determined by measuring titer of an anti-HTLV-1 antibody in the serum, using methods known in the

art, such as, for example, by commercially-available tests such as INNO-LIA™ HTLV I/II (Innogenetics; Gent Belgium) and Abbott HTLV-I/HTLV-II EIA (Abbott Laboratories; Abbott Park, IL). In some instances an effective amount of a composition of the invention is an amount that is sufficient to reduce the titer of an anti-HTLV-1 antibody in the serum to 50%, 25%, 10% or 5% of the titer present prior to the start of treatment. In some instances an effective amount of a composition of the invention is an amount that is sufficient to reduce the titer of an anti-HTLV-1 antibody in the serum to a level which is essentially undetectable. The invention includes a method of reducing the titer of an anti-HTLV-1 antibody in the serum of a patient infected with HTLV-1, comprising administering to the patient a composition of the invention in an amount effective to reduce the titer of the anti-HTLV-1 antibody in the serum compared to that present prior to the start of treatment.

Human Papillomavirus

In another aspect the invention provides a method of treating a patient infected with Human Papillomavirus (HPV), or a disease or condition associated with HPV infection, such as, for example, warts of the hands and feet, and lesions of the mucous membranes of the oral, anal and genital cavities. While many types of HPV are relatively harmless, many other types are spread through sexual contact and give rise to genital or venereal warts (termed condylomata acuminata) which may give rise to cervical cancer and other genital cancers. The method comprises administering to the patient infected with HPV an effective amount of a composition of the invention comprising one or more polypeptide or conjugate of the invention. The invention also provides a composition for use in treating a patient infected with HPV, or a disease or condition associated with HPV infection, the composition comprising one or more polypeptide or conjugate of the invention and a pharmaceutically acceptable carrier or excipient. A patient diagnosed with HPV infection includes a patient exhibiting HPV viral DNA in biopsied genital tissue, and sometimes (but not always) exhibiting visible lesions on genital tissues.

A composition comprising a polypeptide of the invention will generally be administered at a dose and frequency similar to what is employed in HPV therapeutic regimens using clinically-approved interferon-alpha polypeptides, such as, for example, INTRON® A (Interferon alfa-2b, recombinant; Schering Corporation). A recommended

dose of INTRON A for the treatment of condylomata acuminata is 1.0 million IU injected into each lesion, for up to 5 lesions, using a tuberculin or similar syringe and a 25-to 30-gauge needle, three times per week on alternate days, for 3 weeks. Patients with 6 to 10 condylomata may receive a second (sequential) course of treatment at the above dosage schedule, to treat up to five additional condylomata per course of treatment. Patients with greater than 10 condylomata may receive additional sequences depending on how large a number of condylomata are present. The interferon may alternatively or in addition be applied topically, e.g. in a cream or ointment form (as described for example in Stentella *et al.* (1996) Clin. Exp. Obstet. Gynecol. 23(1):29-36). Such dosing schedules provide useful ranges for dosage of a polypeptide of the invention for the treatment of HPV infection, or a disease or condition associated with HPV infection such as condylomata acuminata. Depending on a number of factors (including but not limited to the activity and the pharmacokinetics of the polypeptide of the invention and the size, age and health of the patient), the polypeptide of the invention may be administered in lower amounts and/or less frequently than described above. Likewise, a composition comprising a conjugate of the invention will generally be administered, e.g. intralesionally or topically, at a dose effective to reduce the amount of HPV viral DNA in the effected tissues or to reduce the size/or number of genital lesions in the infected individual.

In some instances the polypeptide or conjugate of the invention is administered in combination with one or more additional therapeutic agent(s). For example, the polypeptide or conjugate of the invention may be administered in combination with an anti-HPV therapeutic such as Podofilox (Condylox) and/or Podophyllin (Pododerm, Podocon-25).

The precise amount and frequency of administration of the polypeptide or conjugate of the invention will depend on a number of factors such as the specific activity and the pharmacokinetic properties of the polypeptide or the conjugate, as well as the nature of the condition being treated, among other factors known to those of skill in the art. Normally, the dose should be capable of preventing or lessening the severity or spread of the indication being treated. Such a dose may be termed an "effective" or "therapeutically effective" amount. It will be apparent to those of skill in the art that an effective amount of a polypeptide, conjugate or composition of the invention depends,

inter alia, upon the condition being treated, the dose, the administration schedule, whether the polypeptide or conjugate or composition is administered alone or in combination with other therapeutic agents, the serum half-life and other pharmacokinetic properties of the polypeptide, conjugate or composition, as well as the size, age, and general health of the patient. The dosage and frequency of administration is ascertainable by one skilled in the art using known techniques.

The effectiveness of treatment may be determined by measuring the HPV viral load, such as, for example, measuring the level of HPV viral DNA in biopsied tissue. In some instances, an effective amount of a composition of the invention is one that is sufficient to achieve a reduction in viral load by at least 0.5 log unit, such as at least 1 log unit, at least 2 log units, at least 3 log units, at least 4 log units, at least 5 log units, at least 6 log units, or at least 7 log units over the course of treatment, compared to the viral load prior to treatment. In some instances an effective amount of a composition of the invention is an amount that is sufficient to reduce viral load to levels which are essentially undetectable. The invention includes a method of reducing the level of HPV viral DNA in tissue of a patient infected with HPV, comprising administering to the patient a composition of the invention in an amount effective to reduce the level of HPV viral DNA compared to that present prior to the start of treatment.

The effectiveness of treatment may alternatively or in addition be determined by observing the size or number of genital lesions (condylomata) in the infected individual. In some instances an effective amount of a composition of the invention is an amount that is sufficient to reduce the size and/or number of condylomata in the infected individual. The invention includes a method of reducing reduce the size and/or number of condylomata in a patient infected with HPV, comprising administering to the patient a composition of the invention in an amount effective to reduce the size and/or number of condylomata in the patient compared to those present prior to the start of treatment.

FORMULATIONS AND ROUTES OF ADMINISTRATION

Therapeutic formulations of the polypeptide or conjugate of the invention are typically administered in a composition that includes one or more pharmaceutically acceptable carriers or excipients. Such pharmaceutical compositions may be prepared in a

manner known *per se* in the art to result in a polypeptide pharmaceutical that is sufficiently storage-stable and is suitable for administration to humans or animals.

Drug form

The polypeptide or conjugate of the invention can be used "as is" and/or in a salt form thereof. Suitable salts include, but are not limited to, salts with alkali metals or alkaline earth metals, such as sodium, potassium, calcium and magnesium, as well as e.g. zinc salts. These salts or complexes may by present as a crystalline and/or amorphous structure.

Excipients

"Pharmaceutically acceptable" means a carrier or excipient that at the dosages and concentrations employed does not cause any untoward effects in the patients to whom it is administered. Such pharmaceutically acceptable carriers and excipients are well known in the art (see Remington's Pharmaceutical Sciences, 18th edition, A. R. Gennaro, Ed., Mack Publishing Company (1990); Pharmaceutical Formulation Development of Peptides and Proteins, S. Frokjaer and L. Hovgaard, Eds., Taylor & Francis (2000) ; and Handbook of Pharmaceutical Excipients, 3rd edition, A. Kibbe, Ed., Pharmaceutical Press (2000)).

Mix of drugs

The composition of the invention may be administered alone or in conjunction with other therapeutic agents. Ribavirin, for example, is often co-administered with IFN-alpha and has been shown to increase efficacy in antiviral treatments, such as HCV treatment. A variety of small molecules are being developed against both viral targets (viral proteases, viral polymerase, assembly of viral replication complexes) and host targets (host proteases required for viral processing, host kinases required for phosphorylation of viral targets such as NS5A and inhibitors of host factors required to efficiently utilize the viral IRES). Other cytokines may be co-administered, such as for example IL-2, IL-12, IL-23, IL-27, or IFN-gamma. These agents may be incorporated as part of the same pharmaceutical composition or may be administered separately from the polypeptide or conjugate of the invention, either concurrently or in accordance with another treatment schedule. In addition, the polypeptide, conjugate or composition of the invention may be used as an adjuvant to other therapies.

Patients

A "patient" for the purposes of the present invention includes both humans and other mammals. Thus the methods are applicable to both human therapy and veterinary applications.

Types of composition and administration route

The pharmaceutical composition comprising the polypeptide or conjugate of the invention may be formulated in a variety of forms, e.g. as a liquid, gel, lyophilized, or as a compressed solid. The preferred form will depend upon the particular indication being treated and will be apparent to one skilled in the art.

The administration of the formulations of the present invention can be performed in a variety of ways, including, but not limited to, orally, subcutaneously, intravenously, intracerebrally, intranasally, transdermally, intraperitoneally, intramuscularly, intrapulmonary, vaginally, rectally, intraocularly, or in any other acceptable manner. The formulations can be administered continuously by infusion, although bolus injection is acceptable, using techniques well known in the art, such as pumps (e.g., subcutaneous osmotic pumps) or implantation. In some instances the formulations may be directly applied as a solution or spray.

Parenterals

An example of a pharmaceutical composition is a solution designed for parenteral administration. Although in many cases pharmaceutical solution formulations are provided in liquid form, appropriate for immediate use, such parenteral formulations may also be provided in frozen or in lyophilized form. In the former case, the composition must be thawed prior to use. The latter form is often used to enhance the stability of the active compound contained in the composition under a wider variety of storage conditions, as it is recognized by those skilled in the art that lyophilized preparations are generally more stable than their liquid counterparts. Such lyophilized preparations are reconstituted prior to use by the addition of one or more suitable pharmaceutically acceptable diluents such as sterile water for injection or sterile physiological saline solution.

Parenterals may be prepared for storage as lyophilized formulations or aqueous solutions by mixing, as appropriate, the polypeptide having the desired degree of purity with one or more pharmaceutically acceptable carriers, excipients or stabilizers typically employed in the art (all of which are termed "excipients"), for example buffering agents, stabilizing agents, preservatives, isotonifiers, non-ionic detergents, antioxidants and/or other miscellaneous additives.

Buffering agents help to maintain the pH in the range which approximates physiological conditions. They are typically present at a concentration ranging from about 2 mM to about 50 mM. Suitable buffering agents for use with the present invention include both organic and inorganic acids and salts thereof such as citrate buffers (e.g., monosodium citrate-disodium citrate mixture, citric acid-trisodium citrate mixture, citric acid-monosodium citrate mixture, etc.), succinate buffers (e.g., succinic acid-monosodium succinate mixture, succinic acid-sodium hydroxide mixture, succinic acid-disodium succinate mixture, etc.), tartrate buffers (e.g., tartaric acid-sodium tartrate mixture, tartaric acid-potassium tartrate mixture, tartaric acid-sodium hydroxide mixture, etc.), fumarate buffers (e.g., fumaric acid-monosodium fumarate mixture, fumaric acid-disodium fumarate mixture, monosodium fumarate-disodium fumarate mixture, etc.), gluconate buffers (e.g., gluconic acid-sodium glyconate mixture, gluconic acid-sodium hydroxide mixture, gluconic acid-potassium glyuconate mixture, etc.), oxalate buffer (e.g., oxalic acid-sodium oxalate mixture, oxalic acid-sodium hydroxide mixture, oxalic acid-potassium oxalate mixture, etc.), lactate buffers (e.g., lactic acid-sodium lactate mixture, lactic acid-sodium hydroxide mixture, lactic acid-potassium lactate mixture, etc.) and acetate buffers (e.g., acetic acid-sodium acetate mixture, acetic acid-sodium hydroxide mixture, etc.). Additional possibilities are phosphate buffers, histidine buffers and trimethylamine salts such as Tris.

Preservatives are added to retard microbial growth, and are typically added in amounts of about 0.2%-1% (w/v). Suitable preservatives for use with the present invention include phenol, benzyl alcohol, meta-cresol, methyl paraben, propyl paraben, octadecyldimethylbenzyl ammonium chloride, benzalkonium halides (e.g. benzalkonium chloride, bromide or iodide), hexamethonium chloride, alkyl parabens such as methyl or propyl paraben, catechol, resorcinol, cyclohexanol and 3-pentanol.

Isotonicifiers are added to ensure isotonicity of liquid compositions and include polyhydric sugar alcohols, preferably trihydric or higher sugar alcohols, such as glycerin, erythritol, arabitol, xylitol, sorbitol and mannitol. Polyhydric alcohols can be present in an amount between 0.1% and 25% by weight, typically 1% to 5%, taking into account the relative amounts of the other ingredients.

Stabilizers refer to a broad category of excipients which can range in function from a bulking agent to an additive which solubilizes the therapeutic agent or helps to prevent denaturation or adherence to the container wall. Typical stabilizers can be polyhydric sugar alcohols (enumerated above); amino acids such as arginine, lysine, glycine, glutamine, asparagine, histidine, alanine, omithine, L-leucine, 2-phenylalanine, glutamic acid, threonine, etc., organic sugars or sugar alcohols, such as lactose, trehalose, stachyose, mannitol, sorbitol, xylitol, ribitol, myoinisitol, galactitol, glycerol and the like, including cyclitols such as inositol; polyethylene glycol; amino acid polymers; sulfur-containing reducing agents, such as urea, glutathione, thioctic acid, sodium thioglycolate, thioglycerol, α-monothioglycerol and sodium thiosulfate; low molecular weight polypeptides (i.e. <10 residues); proteins such as human serum albumin, bovine serum albumin, gelatin or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; monosaccharides such as xylose, mannose, fructose and glucose; disaccharides such as lactose, maltose and sucrose; trisaccharides such as raffinose, and polysaccharides such as dextran. Stabilizers are typically present in the range of from 0.1 to 10,000 parts by weight based on the active protein weight.

Non-ionic surfactants or detergents (also known as "wetting agents") may be present to help solubilize the therapeutic agent as well as to protect the therapeutic polypeptide against agitation-induced aggregation, which also permits the formulation to be exposed to shear surface stress without causing denaturation of the polypeptide. Suitable non-ionic surfactants include polysorbates (20, 80, etc.), polyoxamers (184, 188 etc.), Pluronic® polyols, polyoxyethylene sorbitan monoethers (Tween®-20, Tween®-80, etc.).

Additional miscellaneous excipients include bulking agents or fillers (e.g. starch), chelating agents (e.g. EDTA), antioxidants (e.g., ascorbic acid, methionine, vitamin E) and cosolvents.

The active ingredient may also be entrapped in microcapsules prepared, for example, by coascervation techniques or by interfacial polymerization, for example

hydroxymethylcellulose, gelatin or poly-(methylmethacylate) microcapsules, in colloidal drug delivery systems (for example liposomes, albumin microspheres, microemulsions, nano-particles and nanocapsules) or in macroemulsions. Such techniques are disclosed in Remington's Pharmaceutical Sciences, *supra*.

Parenteral formulations to be used for *in vivo* administration must be sterile. This is readily accomplished, for example, by filtration through sterile filtration membranes.

Sustained release preparations

Suitable examples of sustained-release preparations include semi-permeable matrices of solid hydrophobic polymers containing the polypeptide or conjugate, the matrices having a suitable form such as a film or microcapsules. Examples of sustained-release matrices include polyesters, hydrogels (for example, poly(2-hydroxyethyl-methacrylate) or poly(vinylalcohol)), polylactides, copolymers of L-glutamic acid and ethyl-L-glutamate, non-degradable ethylene-vinyl acetate, degradable lactic acid-glycolic acid copolymers such as the ProLease® technology or Lupron Depot® (injectable microspheres composed of lactic acid-glycolic acid copolymer and leuprolide acetate), and poly-D-(-)-3-hydroxybutyric acid. While polymers such as ethylene-vinyl acetate and lactic acid-glycolic acid enable release of molecules for long periods such as up to or over 100 days, certain hydrogels release proteins for shorter time periods. When encapsulated polypeptides remain in the body for a long time, they may denature or aggregate as a result of exposure to moisture at 37°C, resulting in a loss of biological activity and possible changes in immunogenicity. Rational strategies can be devised for stabilization depending on the mechanism involved. For example, if the aggregation mechanism is discovered to be intermolecular S-S bond formation through thio-disulfide interchange, stabilization may be achieved by modifying sulfhydryl residues, lyophilizing from acidic solutions, controlling moisture content, using appropriate additives, and developing specific polymer matrix compositions.

Oral administration

For oral administration, the pharmaceutical composition may be in solid or liquid form, e.g. in the form of a capsule, tablet, suspension, emulsion or solution. The pharmaceutical composition is preferably made in the form of a dosage unit containing a

given amount of the active ingredient. A suitable daily dose for a human or other mammal may vary widely depending on the condition of the patient and other factors, but can be determined by persons skilled in the art using routine methods.

Solid dosage forms for oral administration may include capsules, tablets, suppositories, powders and granules. In such solid dosage forms, the active compound may be admixed with at least one inert diluent such as sucrose, lactose, or starch. Such dosage forms may also comprise, as is normal practice, additional substances, e.g. lubricating agents such as magnesium stearate. In the case of capsules, tablets and pills, the dosage forms may also comprise buffering agents. Tablets and pills can additionally be prepared with enteric coatings.

The polypeptides or conjugates may be admixed with adjuvants such as lactose, sucrose, starch powder, cellulose esters of alkanoic acids, stearic acid, talc, magnesium stearate, magnesium oxide, sodium and calcium salts of phosphoric and sulphuric acids, acacia, gelatin, sodium alginate, polyvinyl-pyrrolidine, and/or polyvinyl alcohol, and tableted or encapsulated for conventional administration. Alternatively, they may be dissolved in saline, water, polyethylene glycol, propylene glycol, ethanol, oils (such as corn oil, peanut oil, cottonseed oil or sesame oil), tragacanth gum, and/or various buffers. Other adjuvants and modes of administration are well known in the pharmaceutical art. The carrier or diluent may include time delay material, such as glyceryl monostearate or glyceryl distearate alone or with a wax, or other materials well known in the art.

The pharmaceutical compositions may be subjected to conventional pharmaceutical operations such as sterilization and/or may contain conventional adjuvants such as preservatives, stabilizers, wetting agents, emulsifiers, buffers, fillers, etc., e.g. as disclosed elsewhere herein.

Liquid dosage forms for oral administration may include pharmaceutically acceptable emulsions, solutions, suspensions, syrups and elixirs containing inert diluents commonly used in the art, such as water. Such compositions may also comprise adjuvants such as wetting agents, sweeteners, flavoring agents and perfuming agents.

Pulmonary delivery

Formulations suitable for use with a nebulizer, either jet or ultrasonic, will typically comprise the polypeptide or conjugate dissolved in water at a concentration of, e.g., about

0.01 to 25 mg of conjugate per mL of solution, preferably about 0.1 to 10 mg/mL. The formulation may also include a buffer and a simple sugar (e.g., for protein stabilization and regulation of osmotic pressure), and/or human serum albumin ranging in concentration from 0.1 to 10 mg/ml. Examples of buffers that may be used are sodium acetate, citrate and glycine. Preferably, the buffer will have a composition and molarity suitable to adjust the solution to a pH in the range of 3 to 9. Generally, buffer molarities of from 1 mM to 50 mM are suitable for this purpose. Examples of sugars which can be utilized are lactose, maltose, mannitol, sorbitol, trehalose, and xylose, usually in amounts ranging from 1% to 10% by weight of the formulation.

The nebulizer formulation may also contain a surfactant to reduce or prevent surface induced aggregation of the protein caused by atomization of the solution in forming the aerosol. Various conventional surfactants can be employed, such as polyoxyethylene fatty acid esters and alcohols, and polyoxyethylene sorbitan fatty acid esters. Amounts will generally range between 0.001% and 4% by weight of the formulation. An especially preferred surfactant for purposes of this invention is polyoxyethylene sorbitan monooleate.

Specific formulations and methods of generating suitable dispersions of liquid particles of the invention are described in WO 94/20069, US 5,915,378, US 5,960,792, US 5,957,124, US 5,934,272, US 5,915,378, US 5,855,564, US 5,826,570 and US 5,522,385 which are hereby incorporated by reference.

Formulations for use with a metered dose inhaler device will generally comprise a finely divided powder. This powder may be produced by lyophilizing and then milling a liquid conjugate formulation and may also contain a stabilizer such as human serum albumin (HSA). Typically, more than 0.5% (w/w) HSA is added. Additionally, one or more sugars or sugar alcohols may be added to the preparation if necessary. Examples include lactose maltose, mannitol, sorbitol, sorbitose, trehalose, xylitol, and xylose. The amount added to the formulation can range from about 0.01 to 200% (w/w), preferably from approximately 1 to 50%, of the conjugate present. Such formulations are then lyophilized and milled to the desired particle size.

The properly sized particles are then suspended in a propellant with the aid of a surfactant. The propellant may be any conventional material employed for this purpose, such as a chlorofluorocarbon, a hydrochlorofluorocarbon, a hydrofluorocarbon, or a

hydrocarbon, including trichlorofluoromethane, dichlorodifluoromethane, dichlorotetrafluoroethanol, and 1,1,1,2-tetrafluoroethane, or combinations thereof. Suitable surfactants include sorbitan trioleate and soya lecithin. Oleic acid may also be useful as a surfactant. This mixture is then loaded into the delivery device. An example of a commercially available metered dose inhaler suitable for use in the present invention is the Ventolin metered dose inhaler, manufactured by Glaxo Inc., Research Triangle Park, NC, USA.

Formulations for powder inhalers will comprise a finely divided dry powder containing conjugate and may also include a bulking agent, such as lactose, sorbitol, sucrose, or mannitol in amounts which facilitate dispersal of the powder from the device, e.g., 50% to 90% by weight of the formulation. The particles of the powder shall have aerodynamic properties in the lung corresponding to particles with a density of about 1 g/cm^2 having a median diameter less than 10 micrometers, preferably between 0.5 and 5 micrometers, most preferably of between 1.5 and 3.5 micrometers. An example of a powder inhaler suitable for use in accordance with the teachings herein is the Spinhaler powder inhaler, manufactured by Fisons Corp., Bedford, MA, USA.

The powders for these devices may be generated and/or delivered by methods disclosed in US 5,997,848, US 5,993,783, US 5,985,248, US 5,976574, US 5,922,354, US 5,785,049 and US 5,654,007.

Mechanical devices designed for pulmonary delivery of therapeutic products, include but are not limited to nebulizers, metered dose inhalers, and powder inhalers, all of which are familiar to those of skill in the art. Specific examples of commercially available devices suitable for the practice of this invention are the Ultravent nebulizer, manufactured by Mallinckrodt, Inc., St. Louis, MO, USA; the Acorn II nebulizer, manufactured by Marquest Medical Products, Englewood, CO, USA; the Ventolin metered dose inhaler, manufactured by Glaxo Inc., Research Triangle Park, NC, USA; the Spinhaler powder inhaler, manufactured by Fisons Corp., Bedford, MA, USA the "standing cloud" device of Nektar Therapeutics, Inc., San Carlos, CA, USA; the AIR inhaler manufactured by Alkermes, Cambridge, MA, USA; and the AERx pulmonary drug delivery system manufactured by Aradigm Corporation, Hayward, CA, USA.

KITS

The present invention also provides kits including the polypeptides, conjugates, polynucleotides, expression vectors, cells, methods, compositions, and systems, and apparatuses of the invention. Kits of the invention optionally comprise at least one of the following of the invention: (1) an apparatus, system, system component, or apparatus component as described herein; (2) at least one kit component comprising a polypeptide or conjugate or polynucleotide of the invention; a plasmid expression vector encoding a polypeptide of the invention; a cell expressing a polypeptide of the invention; or a composition comprising at least one of any such component; (3) instructions for practicing any method described herein, including a therapeutic or prophylactic method, instructions for using any component identified in (2) or any composition of any such component; and/or instructions for operating any apparatus, system or component described herein; (4) a container for holding said at least one such component or composition, and (5) packaging materials.

In a further aspect, the present invention provides for the use of any apparatus, component, composition, or kit described above and herein, for the practice of any method or assay described herein, and/or for the use of any apparatus, component, composition, or kit to practice any assay or method described herein.

EXAMPLES

The following examples are offered to illustrate the present invention, but not to limit the spirit or scope of the present invention in any way.

MATERIALS AND METHODS

I. DETERMINATION OF SURFACE-ACCESSIBLE RESIDUES

Accessible Surface Area (ASA)

The computer program Access (B. Lee and F.M. Richards, J. Mol. Biol. 55: 379-400 (1971)) version 2 (©1983 Yale University) was used to compute the accessible surface area (ASA) of the individual atoms in the structure. This method typically uses a probe-size of 1.4 Å and defines the Accessible Surface Area (ASA) as the area formed by the center of the probe. Prior to this calculation all water molecules and all hydrogen atoms

should be removed from the coordinate set, as should other atoms not directly related to the protein.

Fractional ASA of side chain

The fractional ASA of the side chain atoms is computed by division of the sum of the ASA of the atoms in the side chain by a value representing the ASA of the side chain atoms of that residue type in an extended ALA-x-ALA tripeptide. See Hubbard, Campbell & Thornton (1991) *J. Mol. Biol.* 220, 507-530. For this example the CA atom is regarded as a part of the side chain of glycine residues but not for the remaining residues. The following values are used as standard 100% ASA for the side chain (Table 6):

Ala	69.23	Å^2	Leu	140.76	Å^2
Arg	200.35	Å^2	Lys	162.50	Å^2
Asn	106.25	Å^2	Met	156.08	Å^2
Asp	102.06	Å^2	Phe	163.90	Å^2
Cys	96.69	Å^2	Pro	119.65	Å^2
Gln	140.58	Å^2	Ser	78.16	Å^2
Glu	134.61	Å^2	Thr	101.67	Å^2
Gly	32.28	Å^2	Trp	210.89	Å^2
His	147.00	Å^2	Tyr	176.61	Å^2
Ile	137.91	Å^2	Val	114.14	Å^2

Residues not detected in the structure are defined as having 100% exposure as they are thought to reside in flexible regions. In the case where an ensemble of NMR structures is analyzed, the average ASA value of the ensemble is used.

Determination of surface exposed residues when no three-dimensional structure is available:

When no three-dimensional structure is available or if the structure is not detailed enough to determine surface accessibility (e.g. if only the position of the CA atoms is known) the surface accessibility may be inferred from a sequence alignment created as follows:

A: If the structure is known but not detailed enough to determine surface accessibility:

The low detail structure is included in a structure-based sequence alignment to the known structures of the sequence family using the MODELER program available from Molecular Simulations, Inc.

B: If no structure is known:

The sequence is aligned to a predefined sequence alignment, including the sequences of the known structures of the sequence family, that may be prepared using the "profile/structure alignment" option of the program ClustalW (Thompson et al. (1994) *Nucleic Acids Research* 22:4673-4680).

From the sequence alignment obtained in A or B, residues in the sequence to be analyzed at positions equivalent to residues exposed in at least one of the other sequences having a known structure are defined as being exposed. The degree of exposure is taken to be the largest value for the equivalent residues in the other sequences. In cases where the sequence to be analyzed is at an insertion (i.e. there are no equivalent residues in the other sequences) this residue is defined as being fully exposed, as it most probably is located in a turn/loop region. In cases where a low detailed structure exists, those residues not observed in the structure are defined as being fully exposed, as they are thought to be in flexible regions.

Determining distances between atoms:

The distance between atoms is readily determined using molecular graphics software, e.g. InsightII® 98.0 from Molecular Simulations, Inc.

II. PROTEIN EXPRESSION AND PURIFICATION

Shuffled interferon-alpha polypeptide coding sequence was PCR-amplified using Herculase (Stratagene) or Phusion (Finnzyme) polymerases to introduce NdeI and NotI restriction sites in the flanking regions. The PCR product was purified with the Qiagen PCR-purification kit, digested with NdeI and NotI enzymes (NEB), and separated on a 1% agarose gel. The appropriate band (~520 bp) was excised and DNA extracted with the Qiagen Gel-extraction kit. The insert DNA thus obtained was ligated into a derivative of the pCMV-Mkan vector (Punnonen J. *et al.* , PCT Publication WO 2004/007664) which contains a CMV promoter to drive interferon expression, an IFNα5-like signal sequence at the N-terminus of the insert, an E-tag (GAPVPYPDPLEPR; SEQ ID

NO:334) and an S-tag (KETAAAKFERQHMDS; SEQ ID NO:335) at the C-terminus of the insert, and a kanamycin marker for selection in *E.coli*. The resulting ligation was desalted with the Qiagen PCR-purification kit, resuspended in a 10mM Tris pH 8.0 buffer and 1-2 µl were electroporated into XL1-Blue Electroporation competent cells (Stratagene) as specified by the supplier.

One day prior to transfection, 5-8 x 10^6 COS-7 cells were seeded in a T175 flask in 35 ml of DMEM supplemented with antibiotics and 10% Fetal Bovine Serum (FBS; Hyclone). Just prior to the transfection, the medium was aspirated and replaced with 35 ml of OptiMEM (Gibco/Invitrogen) supplemented with antibiotics after a single rinse with 10 ml of OptiMEM. For each T175 flask, the transfection mix was prepared as follows: 1 ml OptiMEM + 50ul Fugene6 Transfection Reagent (Roche Diagnostics) was incubated for 5 min at room temperature at which time 10 µg of endotoxin-free DNA (Qiagen endotoxin-free maxiprep, prepared as described in the protocol provided by the manufacturer) was added and the mix was incubated for a further 30 min at room temperature before being added to the cells. The crude supernatant was harvested at 24h, clarified by centrifugation at 1000 rpm for 10 min and stored at –80°C.

The interferon polypeptide was purified from the crude supernatant using the AKTA Explorer HPLC system (Amersham). About 140 ml (the supernatant from four T175 flasks) was loaded on an E-tag column (RPAS Purification module, Amersham 71-5000-87) that had been equilibrated with PBS. The column was washed first with 4 column volumes of PBS pH 7.4, followed by 3 column volumes of Buffer B1 (20 mM NaOAc, 150 mM NaCl, 1 mM EDTA, pH 5.0). The protein was eluted using a step elution of low-pH Buffer B2 (30 mM citric acid, 150mM NaCl, 1mM EDTA, pH 3.0) for 3 column volumes. The major UV-absorbing peak (approx. 6 ml) was collected in 700 µl of 1 M Tris pH 8.0 to neutralize the pH, and stored at 4°C. The protein sample was buffer-exchanged to 20 mM Tris pH 8.0 in Sterile Water For Irrigation (WFI; B. Braun Medical Inc.) by dialysis using a 10 kDa MWCO Pierce dialysis cassette / slide and subsequently concentrated using an Amicon unit (10 kDa MWCO) by centrifugation at 3500 rpm for 15 mins at 4°C. The protein concentration was measured using the BCA protein assay kit using BSA (Pierce cat #23210) as a standard and formulated in 5%BSA / PBS pH 6.5 and aliquoted for storage at –80°C.

III. ACTIVITY ASSAYS

IFNAR Binding Assay

Binding of an interferon-alpha polypeptide to the human interferon-alpha receptor (IFNAR) may be determined using a flow cytometric competitive binding assay employing a human lymphoma cell line (Daudi) as an IFNAR-expressing cell source, a biotinylated IFN-alpha reference polypeptide as tracer, and phycoerythrin-conjugated streptavidin (SA-PE) for detection.

Briefly, Daudi cells are incubated with various concentrations of the un-labelled polypeptide to be tested ("competitor" polypeptide) for approximately four hours in the presence of a biotinylated IFN-alpha reference polypeptide ("tracer" polypeptide) at a fixed concentration equal to its K_D. The amount of tracer polypeptide which remains bound to IFNAR at each concentration of competitor polypeptide is then determined by staining with SA-PE and assessing by flow cytometry. The concentration of competitor polypeptide that reduces the tracer binding by 50% (the EC_{50} value) is directly related to the intrinsic binding affinity of the competitor polypeptide for the interferon-alpha receptor.

The Daudi human B cell lymphoma cell line may be obtained from the American Tissue Culture Collection (ATCC #CCL-213). Competition binding assays are performed on Daudi cells that are maintained in culture for less than 30 days. The Daudi cells are cultured in complete RPMI1640 medium (BioWhittaker #BE12-702F/U1) containing 10% fetal bovine serum (Hyclone, #SH30071.03), glucose 4.5 g/L (Sigma #G8769, 450 g/L), sodium pyruvate 1 mM (Gibco, #11360-039, 100 mM), penicillin (100 U/ml) and streptomycin (100 mg/ml). The cells are maintained in a 37°C humidified incubator with 5% CO_2 at a cell density between 0.5×10^6 and 2×10^6 cells/mL by the addition of fresh medium 2-3 times a week and replacement of medium once a week.

Tracer polypeptide is prepared by biotinylation of an IFN-alpha reference polypeptide (such as, for example, human IFN-alpha 2a) using the EZ-Link® NHS-PEO Solid Phase Biotinylation Kit (Pierce Biotechnology, Inc., product # 21450) using the protocol provided by the manufacturer. The moles of biotin per mole of tracer polypeptide is quantitated using the EZ Biotin Quantitation Kit (Pierce Biotechnology,

Inc., product # 28005) using the protocol provided by the manufacturer. The K_D of tracer polypeptide binding to Daudi cells is determined by incubating Daudi cells with varying amounts of tracer polypeptide and treating the cells with SA-PE (available from BD Pharmingen, product #554061 or Dako, product #R0438). The mean fluorescence intensity (MFI) for a particular concentration of tracer is representative of the amount of bound ligand per cell. The background detected with SA-PE alone is subtracted from the MFI values obtained and these values are then plotted versus concentration of tracer to yield a saturation-binding curve from which the K_D is calculated using non-linear regression, one-site curve fitting. This K_D is used as the concentration of tracer in subsequent competitive binding assays.

For the competition binding assay, Daudi cells are plated at a density of 200,000 cells per 50 ul per well in a 96-well round bottom assay plate (such as VWR, #29442-066) in phosphate buffered saline (PBS) plus 2% fetal bovine serum (FBS). Between 8 and 12 two-fold dilutions of the competitor polypeptide, ranging from, for example, 4 μM to 1 pM, are prepared. One hundred microliters of the diluted 2X competitor preparations are transferred to the cell plates to give a final competitor concentration in each well of, for example, 2 μM to 0.5 pM. Fifty microliters of biotinylated tracer polypeptide at 4X the K_D (as described above) is added to the 150 ul of cells plus competitor, to give a final concentration of 1X the K_D in the assay. The plates are incubated at 4°C for 4 hours with intermittent shaking on an orbital shaker. The cells are then washed with PBS plus 2% FBS before staining is performed using 50 ul of SA-PE (a 25-fold dilution of BD Pharmingen #554061 or a 40-fold dilution of Dako #R0438) for 30 minutes on ice in the dark. Cells are subsequently washed twice with PBS plus 2% FBS before acquisition by flow cytometry (FacsCalibur, BD Bioscience) using a multiwell autosampler (BD Bioscience), CellQuestPro software (BD Bioscience) and multiwell plate manager software, MPM ver3.1 (AMS Cytek or BD Bioscience).

The background MFI (defined as the MFI of cells stained with SA-PE in the absence of tracer or competitor) is subtracted from the MFI generated at each competitor concentration. The resulting values are plotted as a function of the competitor concentration, and EC_{50} values are determined using a non-linear regression one-site competition binding analysis equation.

HeLa-EMCV Antiviral Assay

Provided below is an exemplary assay for antiviral activity of interferon-alpha polypeptides and conjugates of the invention. The assay is a cell-based dose-response assay used to assess the anti-viral potency of a drug, and is sometimes referred to as "protection from cytopathic effect" (or PCPE) assay, also termed inhibition of cytopathic effect (CPE) assay. Briefly, cells are incubated with drug and exposed to virus. In the absense of drug, cells exposed to virus die. With increasing concentrations of drug, an increasing proportion of cells survive. The number of surviving cells can be measured directly (e.g., by visual counts) or indirectly by estimating metabolic rate. For example, metabolic dyes such as MTT or WST-1 may be used as an indirect measure of cell survival. Live cells metabolize such dyes to form metabolic products which can be quantified by spectrophotometry (optical density).

Materials and Reagents:

HeLa Cells: Human cervical carcinoma cell line (ATCC # CCL-2). The HeLa cell line was derived from a cervical adenocarcinoma from a 35-year-old female. The HeLa cells are reported to contain human papilloma virus (HPV-18) sequences. The cell line was received from the ATCC at passage number 107.

L-929 Cells: Murine fibroblast cell line (ATCC # CCL-1). The L-929 cell line is a single cell clone isolated from the 95^{th} passage of the parental strain, Strain L, in 1948. Strain L was isolated from the subcutaneous areolar and adipose tissue of a normal 100 day old male C[3]H/An mouse.

Encephalomyocarditis virus (EMCV): tissue culture adapted strain (ATCC # VR-129B). A tissue culture adapted strain of encephalomyocarditis virus (EMCV) was purchased from the ATCC (# VR-129B). For the HeLa antiviral assay, the high titer EMCV stock was produced in L929 cells. The viral titer of the L929 produced viral stock was 4.0×10^8 PFU/ml based on the results of a plaque assay on L929 cells.

Complete MEM:

Minimal Essential Media (MEM, Gibco Cat. No. 10370-021)

10% Fetal Bovine Serum (FBS, Hyclone Cat. No. SH30071.03)

1x Penicillin-streptomycin-gluatimine (PSG, Gibco Cat. No. 10378-016)

1mM Sodium pyruvate (Gibco Cat. No. #11360-070)

Reduced Serum MEM:

Minimal Essential Media (MEM, Gibco Cat. No. 10370-021)

2% Fetal Bovine Serum (FBS, Hyclone Cat. No. SH30071.03)

1x Penicillin-streptomycin-gluatimine (PSG, Gibco Cat. No. 10378-016)

1mM Sodium pyruvate (Gibco Cat. No. #11360-070)

Trypsin/EDTA (Gibco Cat. No. 25300-054)

WST-1 (Roche; Cat. No. 1 644 807)

HeLa cells were maintained in Complete MEM at 37°C in a humidified 5% CO_2 incubator. The cells were harvested with trypsin and split twice weekly when confluent to a final density of 2-4 x 10^6 cells per 25 ml in a T175 flask. One day prior to the assay, the cells were trypsinized and seeded into new T175 flasks at a density of 6 x 10^6 cells per 25 ml to ensure that the cells were in log phase prior to the assay.

HeLa-EMCV antiviral assay procedure:

On day one of the assay, log phase HeLa cells were harvested with trypsin, resuspended in Reduced Serum MEM and concentrated by centrifugation. The cell pellets, corresponding to 5 T175 flasks of cells, were resuspended in 10 ml of Reduced Serum MEM, filtered through a 40 micron Nylon cell strainer and counted with a Coulter Counter. Cell viability was determined by trypan blue exclusion with a hemocytometer. The cells were resuspended in Reduced Serum MEM to a final density of $1x10^5$ cells/ml. One hundred microliters of the diluted cells were added to each well of a 96-well assay plates ($1x10^4$ cells/well) and the plates were incubated at 37°C in a humidified 5% CO_2 incubator for 24 hours.

The potencies of "reference" interferon alphas and interferon-alpha polypeptides of the invention (also called "test samples") were determined by dose-response analysis. In general, there were 9 test samples and a reference IFN-alpha per plate. Each sample was tested as a single curve on duplicate plates per assay. There were four different references tested per assay, 2 tested in duplicate and one in replicates of 6 to ensure consistent assay quality and performance. Two assays with 2 different operators were performed per week, and two weeks of assays were performed in total, for a total of four separate assays. In each week, the two assays had different arrangements of samples and references per plate, to control for any effects due to sample location. The dose-response curves for the reference IFN-alphas generally consisted of 8 five-fold dilutions, with the

initial dilutions varying, depending on the reference, from 100 ng/ml to 1 ng/ml. The final dilutions would then vary from 0.0013 ng/ml to 0.00001 ng/ml. For the IFN-alpha test samples, the five-fold dilutions ranged from 1 ng/ml to 0.00001 ng/ml. Eight wells of cells were treated with virus but no IFN and eight cells alone were included in each plate as controls.

The IFN-alpha dilutions were prepared using Reduced Serum MEM. One hundred microliters of the diluted IFN-alpha preparations were transferred to the assay plates. The assay plates were incubated at 37°C in a humidified 5% CO_2 incubator for 16 hours.

On day three, the cells were challenged with EMC virus. Medium was aspirated from each well of the assay plate. The EMCV stock was diluted 1:167 in MEM + 2% FBS. One hundred microliters of the diluted virus, corresponding to 3 X 10^5 viral particles was added to each well. The cells were incubated with virus at 37°C in a humidified 5% CO_2 incubator for 24 hours.

On day four, the number of viable cells in each well was quantified by WST-1. The WST-1 reagent was diluted 1:2.3 in Reduced Serum MEM, and 13 μl of the diluted WST-1 reagent was added to each well containing 100 μl of medium plus virus or medium alone, for a final dilution of 1:20. The plates were incubated 37°C in a humidified 5% CO_2 incubator for 60 minutes. The number of viable cells per well was quantified by measuring OD at 450 nm on a plate reader.

Analysis:

The antiviral potency of the IFN-alpha reference and test samples were calculated with the equation:

Antiviral potency =(Viable cells$_{C+I+V}$ – Viable cells$_{C+V}$)/(Viable cells$_{C+I}$-Viable cells$_{C+V}$)*100%

where C+V=cells+EMCV, C+I= cells+IFN-α, and C+I+V= cells+IFN-α+EMCV

Dose-response curves were analyzed by non-linear regression using GraphPad Prism 4 (GraphPad Software Inc.) The following equation was used for the curve fits:

$$Y = \text{Bottom} + \frac{(\text{Top} - \text{Bottom})}{1 + 10^{(\text{LogEC50} - X) \cdot \text{HillSlope}}}$$

Bottom is the Y value at the bottom plateau; Top is the Y value at the top plateau, and LogEC50 is the X value when the response is halfway between Bottom and Top. The Levenberg-Marquardt method was used as optimization algorithm.

T_H1 Differentiation Assay

Provided below is an exemplary assay for T_H1 differentiation activity of interferon-alpha polypeptides and conjugates of the invention.

Assay Procedure:

Human buffy coats (25-30 ml) containing leukocytes and erythrocytes prepared from 500 ml blood were collected from Stanford Blood Bank the day of assay initiation (one day before the assay day) and kept at room temperature overnight. Each buffy coat was carefully transferred to a T75 flask and diluted to 100 ml with PBS. For each buffy coat, 13 ml of Histopaque/Ficoll (Sigma H8889) was pipetted into four 50 ml centrifuge tubes, and 25 ml of diluted blood sample was carefully overlaid on top of the Histopaque/Ficoll without disrupting the interface. The tubes were then centrifuged (20°C, 2500 rpm) for 20 minutes. Using 3 ml plastic transfer pipettes the mononuclear cell layer containing PBMCs was transferred to two 50ml conical tubes (cells from 2 Histopaque/Ficoll/buffy coat tubes to one tube). The PBMCs were then diluted to 50 ml/tube with PBS and centrifuged (20°C, 1000 rpm) for 10 minutes to remove platelets. After removal of PBS, the PBMCs and remaining RBCs were mixed to prevent aggregation. Ten milliliters of RBC lysis buffer (ammonium chloride buffer) were added and two tubes of cells were combined to one tube. Each tube, now containing the total PBMC and RBC isolate from one donor, was incubated at room temperature for 10 min. Potential clots of blood cells were removed by filtering the cells with a cell strainer (70um, Falcon Cat. No. 2350). PBS was added to a total volume of 50 ml followed by centrifugation (20°C, 1000 rpm) for 10min. The cell number was finally counted using a hemocytometer.

Next, a fraction of each PBMC preparation was prestained and analyzed by FACS to select PBMC preparations with a percentage of naïve T_H0 cells above 15%. Three hundred microliters of PBMCs were stained with 20 μl FITC-conjugated anti-human CD45RA (Pharmigen, Cat. No. 555488), 20 μl Cy-chrome conjugated anti-human CD4

(Pharmigen, Cat. No. 555348), 5 μl PE-conjugated anti-human CD8 (Pharmigen, Cat. No. 555367), 5 μl PE-conjugated anti-human CD14 (Pharmigen, Cat. No.555398), and 5 μl PE-conjugated anti-human CD20 (Pharmigen, Cat. No.555623), and incubated on ice for 45 minutes. The cells were washed with PBS, resuspended in 1 ml PBS, and filtered with a 40 μm cell strainer (Falcon, Cat. No. 2340). The percentage of naïve T_H0 cells (positive to CD4 and CD45RA and negative to CD8, CD14, CD20) were quantified by FACS, and PBMC preparations with more than 15% naïve T_H0 cells were selected for the assay.

The selected PBMC preparations were stained with 500 μl FITC-conjugated anti-human CD45RA, 500 μl Cy-chrome conjugated anti-human CD4, 200 μl PE-conjugated anti-human CD8, 50 μl PE-conjugated anti-human CD14, and 50 μl PE-conjugated anti-human CD20, and incubated on ice for 60 minutes. The cells were washed with PBS, PI was added, and the cells were diluted with 10ml of PBS followed by filtering with a 40 μm cell strainer. The cells were FACS sorted, and $1x10^4$ naïve T_H0 cells (positive to CD4 and CD45RA and negative to CD8, CD14, CD20) were transferred by MOFLO into each well of 96 well round bottom plates, containing 160 μl DMEM plus Penicillin-streptomycin plus 2 mM Glutamine and 10% Fetal Bovine Serum (Hyclone Cat. No. SH30071.03).

One point seven microliters of Dynabeads CD3/CD28 T cell expander (Dynal, Cat. No.111.32) were added to each well. The stimulatory effect of the Dynabeads was calibrated prior to the experiment to avoid lot-to-lot variance. Next, 20 μl/well of protein samples were added to the assay plates. Generally, concentration ranges for IL-4 and IL-12 standards (obtained from R&D Systems) were from 0.04 pg/ml to 10 ng/ml, and concentration ranges for IFN-alpha test samples and IFN- alpha reference sample were from 0.76 pg/ml to 200 ng/ml.

The cells were incubated at 37°C in a humidified 5% CO_2 incubator for 6 days. Supernatants from each well were harvested to determine the degree of T_H1 differentiation through quantification of the IFN-γ content, using a standard ELISA (R&D Systems, Cat. # DIF50).

Analysis:

Response = IFN-γ concentrations in pg/ml .

The following equation was used for curve fitting:

$$Y = \text{Bottom} + \frac{(\text{Top} - \text{Bottom})}{1 + 10^{(\text{LogEC50} - X) \cdot \text{HillSlope}}}$$

The variable Bottom is the Y value at the bottom plateau; Top is the Y value at the top plateau, and LogEC50 is the X value when the response is halfway between Bottom and Top. The Levenberg-Marquardt method was used as optimization algorithm.

Daudi Antiproliferation Assay

Provided below is an exemplary assay for antiproliferative activity of interferon-alpha polypeptides and conjugates of the invention.

Materials:

Daudi Cells: Human Burkitt's lymphoma cells (ATCC Number: # CCL-213).

Complete RPMI:

RPMI 1640 (RPMI, Gibco Cat. No. 11875-143)

10% Fetal Bovine Serum (FBS, Hyclone Cat. No. SH30071.03)

1x Penicillin-streptomycin-gluatimine (PSG, Gibco Cat. No. 10378-01

Daudi Burkitt's lymphoma cells grown in suspension were maintained in T175 tissue culture flasks, containing 50ml of complete RPMI at 37°C in a humidified 5% CO_2 incubator. The cells were split 1:10 when confluent.

Assay procedure:

Daudi cells were spun down and washed with 1xPBS. The cell number was adjusted to 10^5 cells/ml. 80 µl culture medium was added to each well in 96 well round bottom assay plates followed by transfer of 100 µl cells (10^4 cells/well) to each well.

Eleven dilutions of the IFN-alpha reference material and IFN-alpha test samples, ranging from 200 ng/ml to 0.2 pg/ml (4-fold dilutions), were prepared in dilution plates using culture medium. Twenty µl of the diluted IFN-alpha preparations were then transferred to the assay plates.

The cells were incubated at 37°C in a humidified 5% CO_2 incubator. After 48 hours, 1µCi of methyl-^{3}H thymidine (Amersham Pharmacia, Cat. No. TRK758) was added to

each well followed by incubation for 24 hours at 37°C in a humidified 5% CO_2 incubator. The cells were harvested on the following day and incorporation of thymidine was determined.

Alternatively, the Daudi antiproliferation assay may be performed by measuring the number of viable, metabolically active Daudi cells based on the amount of ATP present in a culture well following interferon treatment. In this procedure, 8000 Daudi cells are plated in a volume of 50 µl in a 96 well round bottom assay plate. The cells are allowed to incubate at 37°C for 2 hours in a 5% CO_2 incubator prior to the addition of the interferon dilutions. The interferons are diluted 6-fold (9-points) generally starting from 5-10 ng/ml. Following addition of the interferons, the cells are incubated for 72 hours at 37°C in a humidified 5% CO_2 incubator. The number of viable cells in each well is then determined by the addition of 100 µl of CellTiter-Glo™ (Promega, Cat #G7572). The cells plus CellTiter-Glo™ reagent are mixed for 2 minutes and incubated at room temperature in the dark for 30-60 minutes. The amount of luminescent signal for each well is determined using an Analyst HT instrument.

Analysis:

The EC_{50} of the IFN-alpha reference and samples were calculated using the equation:

$$Y = \mathrm{Bottom} + \frac{(\mathrm{Top} - \mathrm{Bottom})}{1 + 10^{(\mathrm{LogEC50} - X) \cdot \mathrm{HillSlope}}}$$

where Bottom is the Y value at the bottom plateau; Top is the Y value at the top plateau, and LogEC50 is the X value when the response is halfway between Bottom and Top. The Levenberg-Marquardt method was used as optimization algorithm.

EXAMPLE 1: DETERMINATION OF SURFACE-ACCESSIBLE RESIDUES OF INTERFERON-ALPHAS

Surface exposure of human interferon-α2a residues:

Based on the 24 NMR structures of human interferon-alpha 2a reported by Klaus et al., *J. Mol. Biol.*, 274: 661-675 (1997), the fractional ASA of side chains was calculated.

The sequence numbering used below is based on the mature sequence of the human interferon-alpha 2a protein (identified herein as SEQ ID NO:322). It is noted that this structure contains two disulphide bridges involving Cys1-Cys98 and Cys29-Cys138, respectively. By computing the ASA and the fractional ASA and taking the average of the 24 structures, focusing on the ASA of the side chains, it was determined that the following residues have more than 25% fractional ASA: D2, L3, P4, Q5, T6, H7, S8, L9, G10, R12, R13, M16, A19, Q20, R22, K23, I24, S25, L26, F27, S28, L30, K31, R33, H34, D35, G37, Q40, E41, E42, G44, N45, Q46, Q48, K49, A50, E51, E58, Q61, Q62, N65, S68, T69, K70, D71, S73, A74, D77, E78, T79, L80, D82, K83, T86, Y89, Q90, N93, D94, E96, A97, V99, I100, Q101, G102, V103, G104, T106, E107, T108, P109, L110, M111, K112, E113, D114, L117, R120, K121, Q124, R125, T127, L128, K131, E132, K133, K134, Y135, S136, P137, C138, A145, M148, R149, S152, L153, N156, Q158, E159, S160, L161, R162, S163, K164 and E165, with position numbering relative to that of the interferon-alpha 2a sequence identified herein as SEQ ID NO:322.

The following residues were determined to have on average more than 50% fractional ASA of their side chain: D2, L3, P4, Q5, T6, H7, S8, L9, R12, R13, M16, A19, S25, F27, S28, K31, R33, H34, D35, G37, E41, G44, N45, Q46, Q48, K49, N65, K70, A74, D77, E78, T79, D82, K83, T86, Y89, Q90, N93, D94, I100, Q101, G102, G104, T106, E107, T108, P109, L110, E113, D114, L117, R120, K121, Q124, R125, L128, K131, E132, K134, P137, R149, E159, L161, R162, S163, K164 and E165, with position numbering relative to that of the interferon-alpha 2a sequence identified herein as SEQ ID NO:322.

Surface exposure of residues corresponding to SEQ ID NO:1:

Owing to an insertion of an amino acid after position 44 of the human interferon-alpha 2 subtypes – such as, for example, interferon-alpha 2b (SEQ ID NO:321) and interferon-alpha 2a (SEQ ID NO:322) -- in many interferon alpha sequences, including all of the known human interferon alpha sequences (apart from the IFN-alpha 2 subtypes) and certain polypeptides of the invention, the position numbering of the surface-exposed residues will be shifted by one residue past position number 44 in, for example, the sequences shown in the alignment Figure 1, relative to the numbering of the sequence denoted hIFNalpha 2b (SEQ ID NO:321).

Based on the above analysis, the following positions, numbered relative to SEQ ID NO:1, are considered to contain amino acid residues having more than 25% fractional ASA: positions 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 13, 16, 19, 20, 22, 23, 24, 25, 26, 27, 28, 30, 31, 33, 34, 35, 37, 40, 41, 42, 44, 46, 47, 49, 50, 51, 52, 59, 62, 63, 66, 69, 70, 71, 72, 74, 75, 78, 79, 80, 81, 83, 84, 87, 90, 91, 94, 95, 97, 98, 100, 101, 102, 103, 104, 105, 107, 108, 109, 110, 111, 112, 113, 114, 115, 118, 121, 122, 125, 126, 128, 129, 132, 133, 134, 135, 136, 137, 138, 139, 146, 149, 150, 153, 154, 157, 159, 160, 161, 162, 163, 164, 165, and 166.

Likewise, the following positions, again numbered relative to SEQ ID NO:1, are considered contain amino acid residues having on average more than 50% fractional ASA of their side chain: 2, 3, 4, 5, 6, 7, 8, 9, 12, 13, 16, 19, 25, 27, 28, 31, 33, 34, 35, 37, 41, 44, 46, 47, 49, 50, 66, 71, 75, 78, 79, 80, 83, 84, 87, 90, 91, 94, 95, 101, 102, 103, 105, 107, 108, 109, 110, 111, 114, 115, 118, 121, 122, 125, 126, 129, 132, 133, 135, 138, 150, 160, 162, 163, 164, 165, and 166.

EXAMPLE 2: ANTIVIRAL ACTIVITES OF INTERFERON-ALPHA POLYPEPTIDES

A major technical challenge with HCV is that the virus cannot be grown *in vitro* and has only recently been cultured in tractable animal models. There are, however, viruses that replicate *in vitro* which are considered to be useful surrogates for HCV viral replication. *In vitro* surrogate assays believed to be predictive of *in vivo* HCV antiviral activity include the assays described in the Materials and Methods section above, which measure the ability of test molecules to protect cells from the cytopathic effect (CPE) of viral infection, using Encephalomyocarditis virus (EMCV) in the human cervical carcinoma-derived HeLa cell line.

Figure 3 shows antiviral activity in a HeLa/EMCV assay, expressed as EC_{50} (ng/ml), for the following exemplary polypeptides of the invention: M04 (SEQ ID NO:262); M05 (SEQ ID NO:266); M23 (SEQ ID NO:232); M45 (SEQ ID NO:88); M01 (SEQ ID NO:312); M20 (SEQ ID NO:297); M27 (SEQ ID NO:167); M09 (SEQ ID NO:107); M02 (SEQ ID NO:208); M33 (SEQ ID NO:94); M37 (SEQ ID NO:141); M30 (SEQ ID NO:46); M22 (SEQ ID NO:171); M24 (SEQ ID NO:310); M44 (SEQ ID NO:176); M31 (SEQ ID NO:26); M10 (SEQ ID NO:89); M14 (SEQ ID NO:296); M03 (SEQ ID

NO:148); M46 (SEQ ID NO:18); M26 (SEQ ID NO:10); M21 (SEQ ID NO:87); M38 (SEQ ID NO:103); M28 (SEQ ID NO:234); M19 (SEQ ID NO:30); M11 (SEQ ID NO:179); M34 (SEQ ID NO:2); M07 (SEQ ID NO:260); M18 (SEQ ID NO:306); M40 (SEQ ID NO:140); M16 (SEQ ID NO:127); M25 (SEQ ID NO:293); M29 (SEQ ID NO:195); M36 (SEQ ID NO:191); M06 (SEQ ID NO:263); M32 (SEQ ID NO:1); M39 (SEQ ID NO:298); M42 (SEQ ID NO:24); M08 (SEQ ID NO:258); M35 (SEQ ID NO:124); M41 (SEQ ID NO:7); M12 (SEQ ID NO:9); M17 (SEQ ID NO:303); and M43 (SEQ ID NO:6), as compared to reference interferon-alpha polypeptides huIFNα-2a (SEQ ID NO:322) and huIFNα-2b (SEQ ID NO:321).

EXAMPLE 3: PEGYLATION OF INTERFERON-ALPHA POLYPEPTIDES

The following provides exemplary procedures for preparing conjugates of the invention.

Cys-PEGylation

A polypeptide of the invention which contains a free cysteine may be cysteine-PEGylated as follows. The polypeptide is first partially reduced with an equimolar concentration of TCEP (Triscarboxyethylphosphine) at 4°C for 30 min in 50 mM MES, 100 mM NaCl, pH 6.0. The reduced polypeptide is then reacted with a 4 fold molar excess of mPEG-MAL reagent (with a PEG moiety such as a 20 kDa or 30 kDa linear mPEG, or a 40 kDa branched mPEG2) for 1h at 4°C under the same conditions. The PEGylated reaction mixture is loaded on to a SP-Sepharose HP column equilibrated with 50mM MES, pH 6.0, 100mM NaCl. After a 10 CV (column volume) wash step a gradient from 0-600 mM NaCl is applied to fractionate the PEGylated and unPEGylated fractions. Fractions are collected and aliquots are analyzed by SDS-PAGE. Fractions containing monoPEGylated species are pooled and formulated for assays for interferon-alpha activity as described above.

N-terminal PEGylation

N-terminal PEGylation with mPEG-butyraldehyde (having a PEG moiety such as a 20 kDa or 30 kDa linear mPEG, or a 40 kDa branched mPEG2) may be performed at 4°C using a 5 fold molar excess of PEG reagent:polypeptide for 4-8 h in 50 mM MES, pH 5.5, 100 mM NaCl, and 20 mM sodium cyanoborohydride, or in 50 mM sodium acetate,

pH 5.5, 100 mM NaCl and 20 mM sodium cyanoborohydride. Conjugates are isolated by chromatography over a SP-Sepharose HP column equilibrated in 50 mM MES pH 5.5, 100 mM NaCl, using a gradient from 100-600 mM NaCl in 50mM MES pH 5.5. Fractions containing monoPEGylated species are pooled and formulated for assays for interferon-alpha activity as described above, and may be further characterized by, for example, using analytical HPLC, amino acid analysis and/or MALDI-TOF mass spectrometry.

Lysine PEGylation

Lysine-PEGylation may be accomplished using a procedure based on that described by Foser et al. (2003) Protein Expression & Purification 30:78-87. Briefly, the polypeptide is reacted with a mPEG-NHS reagent (such as, a 20 kDa or 30 kDa linear mPEG, or a 40 kDa branched mPEG2) at a 1:3 molar ratio of polypeptide:PEG in 50 mM borate buffer, pH 9.0, for 2 h at 4°C. Conjugates are isolated by cation exchange chromatography using SP-Sepharose HP. Fractions containing monoPEGylated species may be pooled and formulated for interferon-alpha activity assays as described above, and may be further characterized by amino acid analysis and/or MALDI-TOF mass spectrometry.

EXAMPLE 4: *IN VIVO* ASSAYS

Measurement of pharmacokinetic (PK) and pharmacodynamic (PD) profiles of a polypeptide or conjugate of the invention

Measurement of biological or serum half-life may be carried out in a number of ways described in the literature. For example, biological half-life may be determined using an ELISA method to detect serum levels of interferon-alpha after e.g. subcutaneous or intramuscular administration. Use of an ELISA method to determine the pharmacokinetics of interferon-alpha administered subcutaneously is e.g. described by Rostaing et al. (1998), J. Am. Soc. Nephrol. 9(12): 2344-48. Merimsky et al. (1991), Cancer Chemother. Pharmacol. 27(5); 406-8, describe the determination of the serum level of an interferon-alpha administered intramuscularly.

For example, the pharmacokinetic (PK) and pharmacodynamic (PD) profiles of a conjugate of the invention may be studied in cynomolgus monkeys (*Macaca fascicularis*) according to the following procdure. Three to four year old female animals with an average weight of 5-6 kg are used in the study. Animals are acclimatized for a minimum of 6 weeks between arrival and start of treatment with a minimum period of 3 weeks acclimatization to the study housing conditions. They are housed singly in stainless-steel mesh cages (at least 540 x 810 x 760 mm) and are kept on an expanded complete commercial primate diet (100 grams/animal/day) analyzed for the absence of chemical and bacterial contaminants. In addition, animals receive fruit daily (apple or banana). Animals are fasted before all procedures requiring anaesthesia.

Three days before study initiation and on the day of study initiation prior to administration of the compounds, blood samples are collected from all animals. Throughout the study, blood samples (1 ml of whole blood) are withdrawn from a femoral or cephalic/saphenous vessel of the unanaesthetised manually restrained animal. The normal feeding regime is maintained during collection. Samples are collected in tubes without anticoagulant, followed by centrifugation at 3000 rpm (about 1760 g) for 10 minutes at 4°C. The serum samples are then separated into two aliquots (approximately 200 µl each) and stored at –20°C.

Prior to initiation of the study, the conjugate of the invention is formulated in 20 mM sodium acetate (pH 6.0) and 140 mM sodium chloride. At study initiation, the conjugate is administered once per animal at either 30 mcg conjugate/kg animal weight (four animals), or 300 mcg/kg (four animals), using a sterile syringe and needle introduced subcutaneously after local disinfection with an aqueous solution of ethyl alcohol. Blood samples are collected at the following time points after administration of the conjugate: 4 hours, 8 hours, 12 hours, 24 hours, 48 hours, 72 hours, 144 hours, 240 hours, 336 hours, 456 hours, 552 hours, 600 hours, 624 hours, 648 hours, 672 hours, 696 hours, 720 hours and 744 hours (or other timepoints as appropriate).

The animals are observed daily to detect any clinical signs or reaction to treatment. Injection sites are visually assessed daily in order to evaluate local tolerance. A detailed clinical examination is performed before the initiation of treatment and at study termination.

The concentration of conjugate in the isolated serum samples are determined after completion of the study, using an ELISA assay. The *in vivo* half-life of the conjugate in cynomolgus monkeys is then determined based on the serum concentration of the compounds at the specified time points.

The pharmacodynamic response in cynomolgus monkeys to treatment with a conjugate of the invention is evaluated by measuring the levels of 2',5'-oligoadenylate synthetase and neopterin in each of the serum samples, using a commercially available RIA (Eiken Chemical Co., Tokyo) and a commercially available ELISA (IBL Immuno Biological Laboratories, Hamburg.), respectively. Based on the measured concentrations of these two biomarkers for interferon activity in the serum samples, the area under the curve (AUC) is determined to quantify the *in vivo* activity of each compound at each of the two dosages.

Determining in vitro immunogenicity

Reduced immunogenicity of a polypeptide or conjugate of the invention relative to a reference molecule can be determined by use of an ELISA method measuring the immunoreactivity of the molecule relative to a reference molecule or preparation, typically a known interferon-alpha protein. The ELISA method is based on antibodies from patients treated with the reference protein. The immunogenicity is considered to be reduced when the polypeptide or conjugate of the invention has a statistically significant lower response in the assay than the reference molecule or preparation.

While the foregoing invention has been described in some detail for purposes of clarity and understanding, it will be clear to one skilled in the art from a reading of this disclosure that various changes in form and detail can be made without departing from the true scope of the invention. It is understood that the examples and embodiments described herein are for illustrative purposes only and that various modifications or changes in light thereof will be suggested to persons skilled in the art and are to be included within the spirit and purview of this application and scope of the appended claims. For example, all the techniques and apparatus described above may be used in various combinations. All publications, patents, patent applications, and/or other documents cited in this application are incorporated herein by reference in their entirety

for all purposes to the same extent as if each individual publication, patent, patent application, and/or other document were individually indicated to be incorporated herein by reference in its entirety for all purposes.

WHAT IS CLAIMED IS:

1. An isolated or recombinant polypeptide comprising a sequence which differs in 0 to 8 amino acid positions from a sequence selected from SEQ ID NO:312; SEQ ID NO:262; SEQ ID NO:266; SEQ ID NO:232; SEQ ID NO:88; SEQ ID NO:297; SEQ ID NO:167; SEQ ID NO:107; SEQ ID NO:208; SEQ ID NO:94; SEQ ID NO:141; SEQ ID NO:46; SEQ ID NO:171; SEQ ID NO:310; SEQ ID NO:176; SEQ ID NO:26; SEQ ID NO:89; SEQ ID NO:296; SEQ ID NO:148; SEQ ID NO:18; SEQ ID NO:10; SEQ ID NO:87; SEQ ID NO:103; SEQ ID NO:234; SEQ ID NO:30; SEQ ID NO:179; SEQ ID NO:2; SEQ ID NO:260; SEQ ID NO:306; SEQ ID NO:140; SEQ ID NO:127; SEQ ID NO:293; SEQ ID NO:195; SEQ ID NO:191; SEQ ID NO:263;SEQ ID NO:1; SEQ ID NO:298; SEQ ID NO:24; SEQ ID NO:258; SEQ ID NO:124; SEQ ID NO:7; SEQ ID NO:9; SEQ ID NO:303; and SEQ ID NO:6, which polypeptide exhibits antiviral activity.

2. The polypeptide of claim 1, comprising a sequence which differs in 0 to 6 amino acid positions from a sequence selected from SEQ ID NO:312; SEQ ID NO:262; SEQ ID NO:266; SEQ ID NO:232; SEQ ID NO:88; SEQ ID NO:297; SEQ ID NO:167; SEQ ID NO:107; SEQ ID NO:208; SEQ ID NO:94; SEQ ID NO:141; SEQ ID NO:46; SEQ ID NO:171; SEQ ID NO:310; SEQ ID NO:176; SEQ ID NO:26; SEQ ID NO:89; SEQ ID NO:296; SEQ ID NO:148; SEQ ID NO:18; SEQ ID NO:10; SEQ ID NO:87; SEQ ID NO:103; SEQ ID NO:234; SEQ ID NO:30; SEQ ID NO:179; SEQ ID NO:2; SEQ ID NO:260; SEQ ID NO:306; SEQ ID NO:140; SEQ ID NO:127; SEQ ID NO:293; SEQ ID NO:195; SEQ ID NO:191; SEQ ID NO:263;SEQ ID NO:1; SEQ ID NO:298; SEQ ID NO:24; SEQ ID NO:258; SEQ ID NO:124; SEQ ID NO:7; SEQ ID NO:9; SEQ ID NO:303; and SEQ ID NO:6.

3. The polypeptide of claim 2, comprising a sequence selected from SEQ ID NO:312; SEQ ID NO:262; SEQ ID NO:266; SEQ ID NO:232; SEQ ID NO:88; SEQ ID NO:297; SEQ ID NO:167; SEQ ID NO:107; SEQ ID NO:208; SEQ ID NO:94; SEQ ID NO:141; SEQ ID NO:46; SEQ ID NO:171; SEQ ID NO:310; SEQ ID NO:176; SEQ ID NO:26; SEQ ID NO:89; SEQ ID NO:296; SEQ ID NO:148; SEQ ID NO:18; SEQ ID NO:10;

SEQ ID NO:87; SEQ ID NO:103; SEQ ID NO:234; SEQ ID NO:30; SEQ ID NO:179; SEQ ID NO:2; SEQ ID NO:260; SEQ ID NO:306; SEQ ID NO:140; SEQ ID NO:127; SEQ ID NO:293; SEQ ID NO:195; SEQ ID NO:191; SEQ ID NO:263;SEQ ID NO:1; SEQ ID NO:298; SEQ ID NO:24; SEQ ID NO:258; SEQ ID NO:124; SEQ ID NO:7; SEQ ID NO:9; SEQ ID NO:303; and SEQ ID NO:6.

4. The polypeptide of claim 1, wherein the antiviral activity of the polypeptide is at least two-fold greater than the antiviral activity of huIFN-alpha 2b or huIFN-alpha 2a in the HeLa/EMCV antiviral assay.

5. A conjugate comprising
(a) the polypeptide of claim 1; and
(b) a non-polypeptide moiety covalently attached to the polypeptide.

6. The conjugate of claim 5, comprising at least two non-polypeptide moieties.

7. The conjugate of claim 5, comprising a non-polypeptide moiety covalently attached to a cysteine residue.

8. The conjugate of claim 5, comprising a non-polypeptide moiety covalently attached to a lysine residue or to the N-terminal amino group.

9. The conjugate of claim 5, comprising a non-polypeptide moiety covalently attached to a lysine residue.

10. The conjugate of claim 5, comprising a non-polypeptide moiety attached to the N-terminal amino group.

11. The conjugate of claim 5, wherein the non-polypeptide moiety is a polyethylene glycol.

12. The conjugate of claim 5, wherein the non-polypeptide moiety is a sugar.

13. The conjugate of claim 5, wherein the sugar is attached to an N-glycosylation site of the polypeptide.

14. A composition comprising the polypeptide of claim 1 and a pharmaceutically acceptable excipient.

15. A composition comprising the conjugate of claim 5 and a pharmaceutically acceptable excipient.

16. An isolated or recombinant polynucleotide comprising a nucleic acid sequence which encodes the polypeptide of claim 1.

17. A host cell comprising the polynucleotide of claim 16.

18. A vector comprising the polynucleotide of claim 16.

19. The vector of claim 18, which is an expression vector comprising the polynucleotide operably linked to a promoter.

20. A host cell comprising the vector of claim 18.

21. A composition comprising the polynucleotide of claim 16 and a pharmaceutically acceptable excipient.

22. A method for preparing the polypeptide of claim 1, the method comprising:

providing a culture comprising a host cell, the host cell comprising an expression vector comprising a promoter operably linked to a polynucleotide, the polynucleotide comprising a nucleic acid sequence which encodes the polypeptide,

culturing the culture under conditions which permit expression of the polypeptide, and recovering the polypeptide.

23. The method of claim 22, wherein the host cell is a eukaryotic host cell.

24. The method of claim 22, wherein the host cell is a bacterial host cell.

25. A method for preparing a conjugate, the method comprising

(i) providing the polypeptide of claim 1, and

(ii) attaching at least one non-polypeptide moiety to the polypeptide, wherein the resulting conjugate exhibits antiviral activity.

26. The method of claim 25, wherein the step of providing the polypeptide comprises:

providing a culture comprising a host cell, the host cell comprising an expression vector comprising a promoter operably linked to a polynucleotide, the polynucleotide comprising a nucleic acid sequence which encodes the polypeptide,

culturing the culture under conditions which permit expression of the polypeptide, and recovering the polypeptide.

27. The method of claim 26, wherein the host cell is a eukaryotic host cell or a bacterial host cell.

28. A method for inhibiting replication of a virus in cells infected with the virus, the method comprising: administering to the cells the polypeptide of claim 1 or the conjugate of claim 5 in an amount effective to inhibit replication of the virus in the cells, thereby inhibiting replication of the virus in said cells.

29. A method for reducing the number of copies of a virus in cells infected with the virus, the method comprising: administering the polypeptide of claim 1 or the conjugate of claim 5 to the cells in an amount effective to reduce the number of copies of the virus in the cells, thereby reducing the number of copies of the virus in said cells.

30. A method for reducing the level of HCV RNA in the serum of a patient infected with HCV, comprising administering to the patient the polypeptide of claim 1 or the conjugate

of claim 5 in an amount effective to reduce the level of HCV RNA compared to the HCV RNA level present prior to the start of treatment.

31. A method for reducing the level of HBV DNA in serum of a patient infected with HBV, comprising administering to the patient the polypeptide of claim 1 or the conjugate of claim 5 in an amount effective to reduce the level of HBV DNA compared to the HBV DNA level present prior to the start of treatment.

32. A method for reducing the level of HIV RNA in serum of a patient infected with HIV, comprising administering to the patient the polypeptide of claim 1 or the conjugate of claim 5 in an amount effective to reduce the level of HIV RNA compared to the HIV RNA level present prior to the start of treatment.

33. The polypeptide of claim 1 or the conjugate of claim 5 for use as a pharmaceutical.

34. Use of the polypeptide of claim 1 or the conjugate of claim 5 for the manufacture of a pharmaceutical for inhibiting replication of a virus in cells infected with the virus.

35. Use of the polypeptide of claim 1 or the conjugate of claim 5 for the manufacture of a pharmaceutical for reducing the number of copies of a virus in cells infected with the virus.

36. Use of the polypeptide of claim 1 or the conjugate of claim 5 for the manufacture of a pharmaceutical for reducing the level of a virus in the serum of a patient infected with the virus.

37. Use according to any of claims 34-36, wherein the virus is HCV, HBV, or HIV.

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                      *        20         *        40         *        60         *        80
SEQ:001    : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFGLPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
hIFNa-1a   : ....E....D...T.M.....S....S...M......F.............P.......L...I....T.K......DED..D.. : 85
hIFNa-2b   : ..........S..T.M.....R...L...........F.....-.......ET.P........I......K......DET..D.. : 84
hIFNa-4b   : .........................H...........F.E.....H....T.................................. : 85
hIFNa-5    : .........S...T.MIM...................F................................K....T.DET..D.. : 85
hIFNa-6    : ..........H..TMM.....R...L..........RF.............E.......V..........K...V..DER..D.L : 85
hIFNa-7    : .........R........................E.RF.E.....H....T.................................. : 85
hIFNa-8b   : .....................R..............EF......DK........................K.....LDET..DE. : 85
hIFNa-10a  : ..................G.................RI............................................... : 85
hIFNa-14a  : .N.S.....N...T.M.M...R..............EF......................M.........KN.....DET..... : 85
hIFNa-16   : .........................H.......Y...F...V.............AF.............K......DET..D.. : 85
hIFNa-17b  : ..................................................T.................................. : 85
hIFNa-21b  : .....................................F................................K....T......... : 85

                 *       100         *       120         *       140         *       160
SEQ:001    : STELYRQLNDLEACVIQEVGVEETPLMNADSILPVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
hIFNa-1a   : C....Q.........M..ER.G...........A................................L.L.....E...... : 166
hIFNa-2b   : Y....Q...........G...T.....KE....A.R...Q......K.....................L.....ES..S.. : 165
hIFNa-4b   : .....Q......................V....A.R...Q..........................L.............D : 166
hIFNa-5    : Y....Q........MM......D.....V....T.R...Q............................L.A...E...... : 166
hIFNa-6    : Y....Q.........M...W.GG.....E....A.R...Q............................S.R...E...... : 166
hIFNa-7    : .....Q......................E.F..A.R...Q......M..........................K.G....D : 166
hIFNa-8b   : YI..DQ......S..M.....I.S...YE....A.R...Q............S...............L.I......KS.. : 166
hIFNa-10a  : .....Q......................E....A.R...Q......I.R.................L.............D : 166
hIFNa-14a  : YI..FQ.M....................E....A.R...Q......M.................................D : 166
hIFNa-16   : YI..FQ.........T.......IA...E....A.R...Q......MG...........................G....D : 166
hIFNa-17b  : .....Q...N..........M.......E....A.R...Q..........................L........I....D : 166
hIFNa-21b  : ....NQ......................V....A.....Q............................L.KIF.E...... : 166
```

Fig. 1

```
                      *        20         *        40         *        60         *        80
SEQ:312    : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFGFPEEEFDGHQFQKTQAISVLHEMIQQTFNLFSTKDSSAAWDERLLEKF : 85
hIFNa-1a   : ....E....D...T.M.....S....S...M........Q.....N....AP.......L...I....T..........D..D.. : 85
hIFNa-2b   : ..........S..T.M.....R...L.............Q...-.N....AET.P........I...............T..D.. : 85
hIFNa-4b   : .........................H............................................E......EQS..... : 84
hIFNa-5    : .........S...T.MIM.....................Q.....N....A........................T...T..D.. : 85
hIFNa-6    : ..........H..TMM.....R...L..........R..Q.....N....AE.......V..............V.......D.L : 85
hIFNa-7    : .........R........................E.R.................................E......EQS..... : 85
hIFNa-8b   : .....................R..............E..Q....DK....A.........................L..T..DE. : 85
hIFNa-10a  : ..................G.................RI.Q.....N....A...................E......EQS..... : 85
hIFNa-14a  : .N.S.....N...T.M.M...R..............E..Q.....N....A.........M..........N.......T..... : 85
hIFNa-16   : .........................H.......Y.....Q.V...N....A....AF......................T..D.. : 85
hIFNa-17b  : .....................................L.Q.....N........................E......EQS..... : 85
hIFNa-21b  : .......................................Q.....N....A........................T.EQS..... : 85

                 *       100         *       120         *       140         *       160
SEQ:312    : YIELDQQLNDLESCVMQEVGVTGTPLMNEDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
hIFNa-1a   : CT..Y.......A.....ER.GE.....A..........R......T...................L.L.....E...... : 166
hIFNa-2b   : .T..Y.......A..I.G....E....K.......R..........K.....................L.....ES..S.. : 165
hIFNa-4b   : ST..Y.......A..I.....EE.....V......R..........T...................L.............D : 166
hIFNa-5    : .T..Y.......A.M......ED.....V....T.R..........T.....................L.A...E...... : 166
hIFNa-6    : .T..Y.......A......W.G.............R..........T.....................S.R...E...... : 166
hIFNa-7    : ST..Y.......A..I.....EE.......F....R.....................................K.G....D : 166
hIFNa-8b   : .....................IES...Y.......R..........T.....S...............L.I......KS.. : 166
hIFNa-10a  : ST..Y.......A..I.....EE............R..........I.R.................L.............D : 166
hIFNa-14a  : ....F..M....A..I.....EE............R............................................D : 166
hIFNa-16   : ....F.......A..T.....EEIA..........R...........G...........................G....D : 166
hIFNa-17b  : ST..Y....N..A..I....MEE............R..........T...................L........I....D : 166
hIFNa-21b  : ST..N.......A..I.....EE.....V.................T.....................L.KIF.E...... : 166
```

Fig. 2

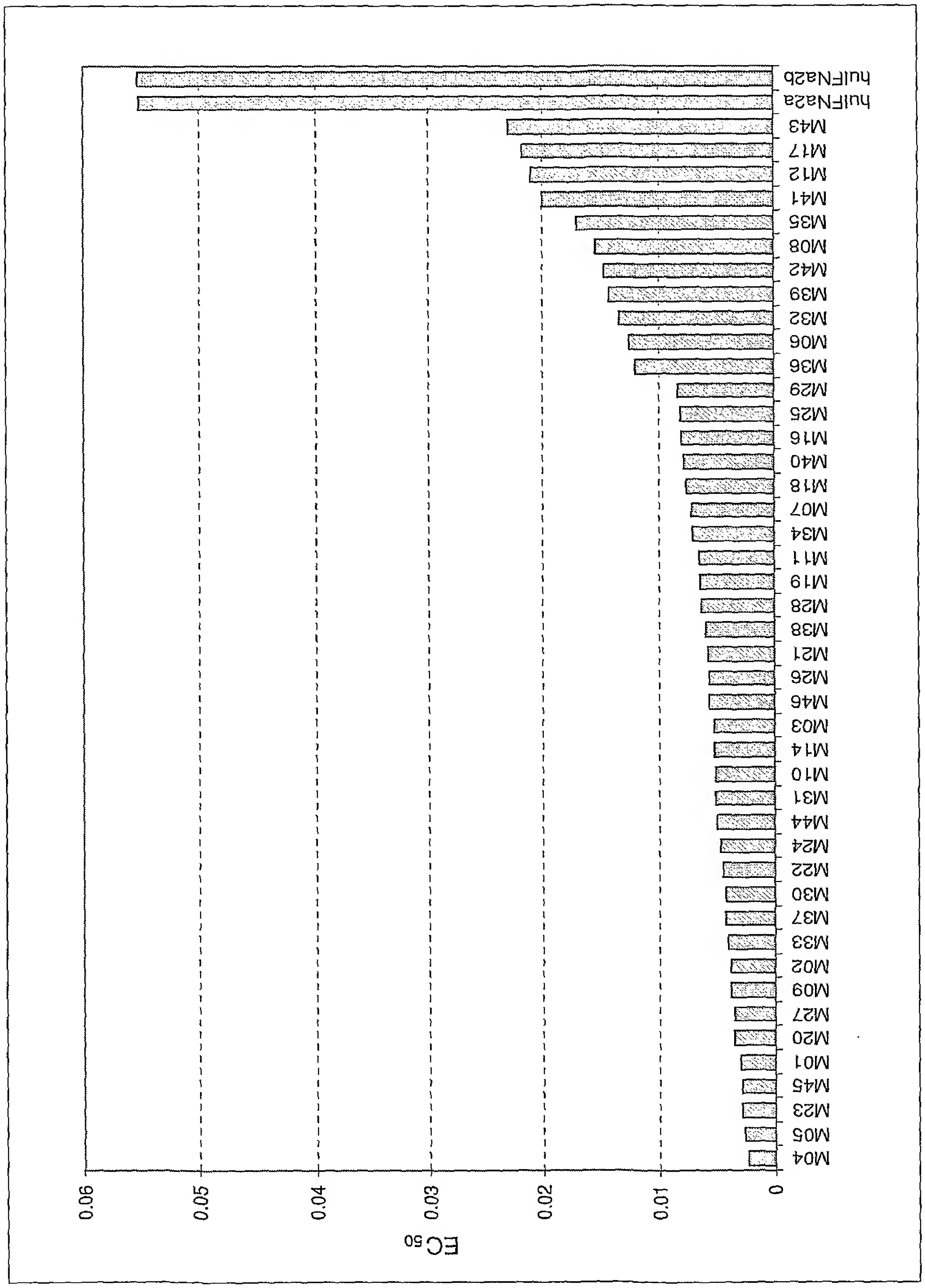
huIFNa2b
huIFNa2a
M43
M17
M12
M41
M35
M08
M42
M39
M32
M06
M36
M29
M25
M16
M40
M18
M07
M34
M11
M19
M28
M38
M21
M26
M46
M03
M14
M10
M31
M44
M24
M22
M30
M37
M33
M02
M09
M27
M20
M01
M45
M23
M05
M04
0.06
0.05
0.04
0.03
0.02
0.01
0
EC_{50}

Fig. 3

BLOSUM62 SUBSTITUTION MATRIX

	A	R	N	D	C	Q	E	G	H	I	L	K	M	F	P	S	T	W	Y	V	B	Z	X	*
A	**4**	-1	-2	-2	0	-1	-1	0	-2	-1	-1	-1	-1	-2	-1	1	0	-3	-2	0	-2	-1	0	-4
R	-1	**5**	0	-2	-3	1	0	-2	0	-3	-2	2	-1	-3	-2	-1	-1	-3	-2	-3	-1	0	-1	-4
N	-2	0	**6**	1	-3	0	0	0	1	-3	-3	0	-2	-3	-2	1	0	-4	-2	-3	3	0	-1	-4
D	-2	-2	1	**6**	-3	0	2	-1	-1	-3	-4	-1	-3	-3	-1	0	-1	-4	-3	-3	4	1	-1	-4
C	0	-3	-3	-3	**9**	-3	-4	-3	-3	-1	-1	-3	-1	-2	-3	-1	-1	-2	-2	-1	-3	-3	-2	-4
Q	-1	1	0	0	-3	**5**	2	-2	0	-3	-2	1	0	-3	-1	0	-1	-2	-1	-2	0	3	-1	-4
E	-1	0	0	2	-4	2	**5**	-2	0	-3	-3	1	-2	-3	-1	0	-1	-3	-2	-2	1	4	-1	-4
G	0	-2	0	-1	-3	-2	-2	**6**	-2	-4	-4	-2	-3	-3	-2	0	-2	-2	-3	-3	-1	-2	-1	-4
H	-2	0	1	-1	-3	0	0	-2	**8**	-3	-3	-1	-2	-1	-2	-1	-2	-2	2	-3	0	0	-1	-4
I	-1	-3	-3	-3	-1	-3	-3	-4	-3	**4**	2	-3	1	0	-3	-2	-1	-3	-1	3	-3	-3	-1	-4
L	-1	-2	-3	-4	-1	-2	-3	-4	-3	2	**4**	-2	2	0	-3	-2	-1	-2	-1	1	-4	-3	-1	-4
K	-1	2	0	-1	-3	1	1	-2	-1	-3	-2	**5**	-1	-3	-1	0	-1	-3	-2	-2	0	1	-1	-4
M	-1	-1	-2	-3	-1	0	-2	-3	-2	1	2	-1	**5**	0	-2	-1	-1	-1	-1	1	-3	-1	-1	-4
F	-2	-3	-3	-3	-2	-3	-3	-3	-1	0	0	-3	0	**6**	-4	-2	-2	1	3	-1	-3	-3	-1	-4
P	-1	-2	-2	-1	-3	-1	-1	-2	-2	-3	-3	-1	-2	-4	**7**	-1	-1	-4	-3	-2	-2	-1	-2	-4
S	1	-1	1	0	-1	0	0	0	-1	-2	-2	0	-1	-2	-1	**4**	1	-3	-2	-2	0	0	0	-4
T	0	-1	0	-1	-1	-1	-1	-2	-2	-1	-1	-1	-1	-2	-1	1	**5**	-2	-2	0	-1	-1	0	-4
W	-3	-3	-4	-4	-2	-2	-3	-2	-2	-3	-2	-3	-1	1	-4	-3	-2	**11**	2	-3	-4	-3	-2	-4
Y	-2	-2	-2	-3	-2	-1	-2	-3	2	-1	-1	-2	-1	3	-3	-2	-2	2	**7**	-1	-3	-2	-1	-4
V	0	-3	-3	-3	-1	-2	-2	-3	-3	3	1	-2	1	-1	-2	-2	0	-3	-1	**4**	-3	-2	-1	-4
B	-2	-1	3	4	-3	0	1	-1	0	-3	-4	0	-3	-3	-2	0	-1	-4	-3	-3	**4**	1	-1	-4
Z	-1	0	0	1	-3	3	4	-2	0	-3	-3	1	-1	-3	-1	0	-1	-3	-2	-2	1	**4**	-1	-4
X	0	-1	-1	-1	-2	-1	-1	-1	-1	-1	-1	-1	-1	-1	-2	0	0	-2	-1	-1	-1	-1	**-1**	-4
*****	-4	-4	-4	-4	-4	-4	-4	-4	-4	-4	-4	-4	-4	-4	-4	-4	-4	-4	-4	-4	-4	-4	-4	**1**

Fig. 4

A.

C	**L**	**K**	**D**	**R**	**H**	**D**	**F**	**G**	L	**P**	Q	**E**	**E**	**F**	**D**	**G**	N	**Q**	**F**	**Q**	**K**			
	L	**K**	**D**	**R**	**H**	**D**	**F**	**G**	F	**P**	E	**E**	**E**	**F**	**D**	**G**	H	**Q**	**F**	**Q**	**K**	T	Q	
	4	5	6	5	8	6	6	6	0	7	2	5	5	6	6	6	1	5	6	5	5			= 105

B.

C	**L**	**K**	**D**	**R**	**H**	**D**	**F**	**G**	**F**	**P**	E	**E**	**E**	**F**	D	G	H	Q	F	Q	K	
	L	**K**	**D**	**R**	**H**	**D**	**F**	**G**	**F**	**P**	Q	**E**	**E**	**F**	G	N	Q	F	Q	K	A	
	4	5	6	5	8	6	6	6	6	7	2	5	5	6	−1	0	0	−3	−3	1	−1	= 70

C.

C	**L**	**K**	**D**	**R**	**H**	**D**	**F**	**G**	**F**	**P**	E	**E**	**E**	**F**	D	**G**	H	**Q**	**F**	**Q**	**K**		
	L	**K**	**D**	**R**	**H**	**D**	**F**	**G**	**F**	**P**	Q	**E**	**E**	**F**	–	**G**	N	**Q**	**F**	**Q**	**K**	A	
	4	5	6	5	8	6	6	6	6	7	2	5	5	6	−12	6	1	5	6	5	5		= 93

Fig. 5

```
                      *         20         *         40         *         60         *         80
SEQ_001 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFGLPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_002 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFGFPQEEFDGNQFQKAQAISVLHELIQQTFNLFSTKNSSAALDETLLDEF : 85
SEQ_003 : CDLPQTHSLGSRRALILLAQMRRISPFSCLKDRHDFGLPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_004 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFGFPQEEFDGNQFQKAQAISVLHELIQQTFNLFSTKNSSAALDETLLDEF : 85
SEQ_005 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFGFPQEEFDGNQFQKAQAISVLHELIQQTFNLFSTKNSSAAWDEDLLDKF : 85
SEQ_006 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFGFPQEEFDGNQFQKAQAISVLHELIQQTFNLFSTKNSSAALDETLLDEF : 85
SEQ_007 : CDLPQTHSLRNRRALILLAQMGRISHFSCLKDRYDFGFPQEEFDGHQFQKTQAISVLHEMIQQTFNLFSTEDSSAAWDETLLDEF : 85
SEQ_008 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFGFPQEEFDGNQFQKAQAISVLHELIQQAFNLFSTKNSSAALDETLLDEF : 85
SEQ_009 : CDLPQTHSLRNRRALILLAQMRRISLFSCLKDRYDFGFPQEEFDGNQFQKAQAISVLHEVIQQTFNLFSTKDSSAAWDETLLDEF : 85
SEQ_010 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRYDFGFPQEEFDGHQFQKTQAISVLHEMIQQTFNLFSTKNSSAAWDEDLLDKF : 85
SEQ_011 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFGFPQEEFDGNQFQKAQAISVLHELIQQTFNLFSTKNSSAALDETLLDEF : 85
SEQ_012 : CDLPQTHSLRNRRTLILLAQMGRISPFSCLKDRHDFGFPQEEFDGNQFQKAPAISVLHEVIQQTFNLFSTKDSSAAWDERLLEKF : 85
SEQ_013 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFGFPQEEFDGNQFQKAQAISVLHELIQQTFNLFSTKDSSAAWDETLLDEF : 85
SEQ_014 : CDLPQTHSLDNRRTLMLLAQMSRISPSSCLMDRHDFGFPQEEFDGNQFQKAQAISAFHEMIQQTFNLFSTKNSSAAWDEDLLDEF : 85
SEQ_015 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHEFRFPEEEFDGHQFQKTQAISVLHEMIQQTFNLFSTKDSSDTWDATLLDEF : 85
SEQ_016 : CDLPQTHSLRNRRALILLARMGRISPFSCLKDRHDFGFPQEEFDGHQFQKTQAISVLHEMIQQTFNLFSTEDSSAAWDETLLDEF : 85
SEQ_017 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRYDFEFPQEEFDGHQFQKAQAISVLHEMMQQTFNLFSTKDSSAAWDETLLDEF : 85
SEQ_018 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFGLPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_019 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFGFPQEEFDGNQFQKAPAISVLHEVIQQTFNLFSTKDSSAAWDETLLDEF : 85
SEQ_020 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHEFRFPEEEFDSNQFQKAQAISVLHEMIQQTFNLFSTKDSSDTWDATLLDEF : 85
SEQ_021 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFGFPQEEFDGNQFQKAQAISVLHELIQQTFNLFSTKNSSAALDETLLDEF : 85
SEQ_022 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFGFPQEEFDGNQFQKAPAISVLHEVIQQTFNLFSTKDSSAAWDATLLDEF : 85
SEQ_023 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFGFPQEEFDGNQFQKAQAISVLHEMIQQTFNLFGTKNSSAAWDEDLLDKF : 85
SEQ_024 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFGFPQEEFDGNQFQKTQAISVLHEMIQQTFNLFSTEDSSAAWDETLLDEF : 85
SEQ_025 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFGFPQEEFDGNQFQKAQAISVLHELIQQTFNLFSTEDSSAAWDETLLDEF : 85
SEQ_026 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFGFPQEEFDGNQFQKAQVISVLHEMIQQTFNLFSTKDSSAAWDETLLDKF : 85
SEQ_027 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFGFPEEEFDGHQFQKTQAISVLHEMIQQTFNLFSTKDSSDTWDATLLDEF : 85
SEQ_028 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFGFPQEEFDGNQFQKAPAISVLHEVIQQTFNLFSTKDSSAAWDETLLDEF : 85
SEQ_029 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFGFPQEEFDSNQFQKAQAISVLHEMIQQTFNLFSTKDSSDTWDETLLDEF : 85
SEQ_030 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHEFRFPEEEFDGHQFQKTQAISVLHEMIQQTFNLFSTKDSSAAWDETLLDEF : 85
```

Fig. 6A

```
                  *        20         *        40         *        60         *        80
SEQ_031 : CDLPQTHSLGNRRAFILLAQMGRISPFSCLKDRHDFGFPQEEFDGSQFQKAQAISVLHEMIQQTFNLFSTKNSSAAWDEDLLDKF : 85
SEQ_032 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFGFPQEEFDGNQFQKAPAISVLHEVIQQTFNLFSTEDSSAAWDETLLDEF : 85
SEQ_033 : CDLPQTHSLRNRRALILLARMGRISPFSCLKDRHDFGFPQEEFDGNQFQKAQAISVLHEMMQQTFNLFSTEDSSAAWDETLLDEF : 85
SEQ_034 : CDLPQTHSLRNRRALILLAQMGRISHFSCLKDRHDFGFPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTKDSSVAWDETLLEKF : 85
SEQ_035 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFGFPQEEFDGNQFQKAPAISVLHEVIQQTFNLFSTKDSSAAWDETLLDEF : 85
SEQ_036 : CDLPQTHSLGNRRAFILLAQMGRISPFSCLKDRHDFGFPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTKNSSAAWDEDLLDEF : 85
SEQ_037 : CDLPQTHSLRNRRALILLAQMGRISHFSCLKDRYDFGFPQEEFDGHQFQKTQAISVLHEMIQQTFNLFSTEDSSAAWDETLLDEF : 85
SEQ_038 : CDLPQTHSLGNRRALILLAQMRRISLFSCLKDRHDFGFPQEEFDGNQFQKAPAISVLHELIQQTFNLFSTKNSSAAWDETLLDEF : 85
SEQ_039 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFGFPEEEFDGHQFQKTQAISVLHEMIQQTFNLFSTKDSSAAWDERLLEKF : 85
SEQ_040 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFGFPEEEFDGHQFQKTQAISVLHEMIQQTFNLFSTKDSSAAWDETLLDEF : 85
SEQ_041 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFGFPQEEFDGNQFQKAQAISVLHELIQQTFNLFSTKDSSAAWDETLLDEF : 85
SEQ_042 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFGFPQEEFDGNQFQKAPAISVLHEVIQQTFNLFSTKDSSAAWDETLLDEF : 85
SEQ_043 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFGFPQEEFDGNQFQKAQAISVLHELIQQTFNLFSTKNSSAALDETLLDEF : 85
SEQ_044 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFGFPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_045 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFGFPQEEFDGNQFQKAPAISVLHEVIQQTFNLFSTKDSSAAWDETLLDEF : 85
SEQ_046 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFGFPEEEFDGHQFQKTQAISVLHEMIQQTFNLFSTKDSSAAWDERLLEKF : 85
SEQ_047 : CDLPQTHSLGNRRAFILLAQMGRISPFSCLKDRHDFGFPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTKNSSAAWDEDLLDKF : 85
SEQ_048 : CDLPQTHSLGHRRTMMLLAQMRRISPFSCLKDRHDFGLPQEEFDGNQFQKAQAISVLHELIQQTFNLFSTKNSSAALDETLLDEF : 85
SEQ_049 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFGFPQEEFDGNQFQKAQAISVLHELIQQTFNLFGTKNSSAALDETLLDEF : 85
SEQ_050 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFGFPQEEFDGNQFQKAPAISVLHEVIQQTFNLFSTKDSSAAWDETLLDEF : 85
SEQ_051 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFGFPQEEFDGNQFQKAPAISVLHEVIQQTFNLFSTKDSSAAWDETLLDEF : 85
SEQ_052 : CDLPQTHSLDNRRTLMLLAQMSRISPSSCLMDRHDFGFPQEVFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSDTWDATLLDKF : 85
SEQ_053 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFGFPEEEFDGNQFQKAQAISVLHEVIQQTFNLFSTKDSSAALDETLLEKF : 85
SEQ_054 : CDLPQTHSLGNRRALILLAQMRRIFPFSCLKDRHDFGFPQEEFDGNQFQKAQAISVLHEMIQRTFNLFSTKDSSATWEQSLLEKF : 85
SEQ_055 : CDLPQTHSLRNRRALILLAQMGRISHFSCLKDRHDFGFPEEEFDGHQFQKAQAISVLHEMIQQTFNLFSTEDSSAAWDETLLEKF : 85
SEQ_056 : CDLPQTHSLGNRRTLMLLAQMSRISPSSCLMDRYDFEFPQEEFG-NQFQKVQAIFLFHEMIQQTFNLFSTKDSSAAWDETLLDKF : 84
SEQ_057 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHEFRFPEEEFDGHQFQKTQAISVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_058 : CDLPQTHSLGNRRALILLGQMGRISPFSCLKDRHDFRIPQEVFDGNQFQKAQAISVLHEMIQQTFNLFSTKDSSAAWEQSLLEKF : 85
SEQ_059 : CDLPQTHSLGHRRTMMLLAQMRRISLFSCLKDRHDFRIPQEEFDGNQFQKAQAISVLHEVIQQTFNLFSTKDSSAAWDETLLDKF : 85
SEQ_060 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFRIPQEEFDGNQFQKAQAISVLHEMMQQTFNLFSTKHSSATWDETLLDKF : 85
```

Fig. 6B

```
                 *        20         *        40         *        60         *        80
SEQ_061 : CDLPQTHSLRSRRTLMLLAQMRRISLFSCLKDRHDFGLPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTKHSSATWDETLLDKF : 85
SEQ_062 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFRIPQEEFDGNQFQKAQAISVLHEMMQQTFNLFSTKHSSATWDETLLDKF : 85
SEQ_063 : CDLPQTHSLRNRRALILLAQMGRISLFSCLKDRHDFRFPQEEFDGNQFQKAEAISVLHEVIQQTFNLFSTEDSSATWEQSLLEKF : 85
SEQ_064 : CDLPQTHSLGNRRALILLAQMGRISLFSCLKDRHDFRFPQEEFG-NQFQKAQAISVLHEMMQQTFNLFSTKNSSAAWDETLLDKL : 84
SEQ_065 : CDLPQTHSLGNRRALILLAQMRRISPFSCLKDRHDFRIPQEEFDGNQFQKAEAISVLHEVIQQTFNLFSTKNSSAAWDEDLLDKF : 85
SEQ_066 : CDLPQTHSLGNRRALILLAQMGRISLFSCLKDRHDFGFPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTKDSSATWEQSLLEKF : 85
SEQ_067 : CDLPQTHSLRNRRALILLAQMGRISLFSCLKDRHDFEFPQEEFDGNQFQKTQAISVLHEMIQQTFNLFSTEDSSAAWDETLLDKF : 85
SEQ_068 : CDLPQTHSLGSRRTLMLLAQMRRISLFSCLKDRHDFEFPQEEFDGNQFQKAQAISAFHEMIQQTFNLFSTKDSSAAWDETLLDKF : 85
SEQ_069 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFRIPQEVFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_070 : CDLPQTHSLGNRRALILLGQMGRISPFSCLKDRHDFRIPQEVFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSAAWDETLLDKL : 85
SEQ_071 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHEFRFPEEEFDGHQFQKTQAISVLHEMIQQTFNLFSTKNSSAAWDEDLLDKF : 85
SEQ_072 : CDLPQTHSLGHRRTMMLLAQMGRISPFSCLKDRHDFRIPQEEFDGHQFQKAQAISVLHEMIQQTFNLFSTEDSSAAWDETLLDKL : 85
SEQ_073 : CDLPQTHSLGNRRALILLAQMGRISLFSCLKDRHDFRFPQEEFDGNQFQKAQAISVLHEVIQQTFNLFSTKDSSAAWDETLLDEF : 85
SEQ_074 : CDLPQTHSLGNRRALILLAQMGRISLFSCLKDRHDFRFPQEEFDSNQFQKAQAISVLHEMIQQTFNLFSTKDSSDTWDATLLDEF : 85
SEQ_075 : CDLPQTHSLGHRRTMMLLAQMRRISLFSCLKDRHDFGFPEEEFDGHQFQKTQAISVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_076 : CDLPQTHSLSNRRAFILLTQMGRISLFSCLKDRHDFGFPEEEFDGHQFQKTQAISVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_077 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFGFPEEEFDGHQFQKTQAISVLHEMIQQTFNLFSTKDSSAAWDERLLEKF : 85
SEQ_078 : CDLPQTHSLGNRRALILLAQMGRISLFSCLKDRHDFGFPEGEFDGNQFQKAQAISVLHEMMQQTFNLFSTKDSSDTWDETLLEKF : 85
SEQ_079 : CDLPQTHSLGNRRALILLAQMGRISLFSCLKDRHDFRFPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_080 : CDLPQTHSLRNRRALILLAQMGRISLFSCLKDRHDFGFPQEEFDGNQFQKAQAISVLHEVIQQTFNLFSTKDSSAAWDETLLDKF : 85
SEQ_081 : CDLPQTHSLSNRRTLILLAQMGRISLFSCLKDRHDFEFPQEEFDDNQFQKAQAISVLHEMMQQTFNLFSTKHSSATWDETLLDKF : 85
SEQ_082 : CDLPQTHSLGNRRALILLAQMGRISLFSCLKDRHDFRFPQEEFDGNQFRKAEAISVLHEVIQQTFNLFSTKDSSAAWDETLLDKF : 85
SEQ_083 : CDLPQTHSLGSRRTLMLLAQMRRISLFSCLKDRHDFEFPQEEFDGNQFQKAQAVSVLHEMIQQTFNLFSTKDSSAAWDETLLDKF : 85
SEQ_084 : CDLPQTHSLGNRRTMMLLAQMRRISLFSCLKDRHDFEFPQEEFDGNQFQKTQAISVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_085 : CDLPQTHSLGNRRALILLGQMGRISPFSCLKDRHDFRIPQEEFDGNQFQKAQAISVLHEMVQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_086 : CDLPQTHSLGNRRALILLAQMGRISLFSCLKDRHDFGFPEEEFDGNQFQKAQAISVLHELIQQTFNLFSTKNSSAAWDETLLDKF : 85
SEQ_087 : CDLPQTHSLGHRRTMMLLAQMGRISPFSCLKDRHDFRIPQEEFDGNQFQKAQAISVLHEMMQQTFNLFSTKHSSAAWDETLLEKF : 85
SEQ_088 : CDLPQTHSLRNRRALILLAQMGRISLFSCLKDRHDFGFPQEEFDGNQFQKTQAISVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_089 : CDLPQTHSLGNRRALILLAQMGRISLFSCLKDRHDFGFPEEEFDGHQVQKVQAIFLFHEVIQQTFNLFSTKHSSAAWDETLLDKF : 85
SEQ_090 : CDLPQTHSLGHRRTMMLLAQMRRISLFSCLKDRHDFGFPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSATWEQSLLEKF : 85
```

Fig. 6C

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                *         20         *         40         *         60         *         80
SEQ_091 : CDLPQTHSLGNRRALILLAQMGRISLFSCLKDRHDFGFPEEEFDGNQFQKAQAISVLHEVIQQTFNLFSTEDSSAAWEQSLLDKF : 85
SEQ_092 : CDLPQTHSLGNRRALILLGQMGRISPFSCLKDRHDFRIPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSAAWDETLLDKF : 85
SEQ_093 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFRIPQEEFDGNQFQKAQAISVLHEMVQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_094 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFGFPEEEFDGHQFQKTQAISVLHEMMQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_095 : CDLPQTHSLGHRRTMMLLAQMRRISLFSCLKDRHDFRFPQEEFDGHQFQKAQAISVLHELIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_096 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFRIPQEEFDGNQFQKAQAISVLHEMVQQTFNLFSTEDSSAAWDETLLDKF : 85
SEQ_097 : CDLPQTHSLGNRRALILLAQMGRISLFSCLKDRHDFGFPEEEFDGHQFQKAEAISVLHEMMQQTFNLFSTEDSSATWDATLLDKF : 85
SEQ_098 : CDLPQTHSLGSRRALILLGQMGRISPFSCLKDRHDFRIPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_099 : CDLPQTHSLGNRRALILLAQMGRISLFSCLKDRHDFRFPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTKDSSDTWDADLLDKF : 85
SEQ_100 : CDLPQTHSLGNRRTMMLLAQMRRISLFSCLKDRHDFGLPQEEFDGHQFQKTQAISVLHELIQQTFNLFSTEDSSATWEQSLLEKF : 85
SEQ_101 : CDLPQTHSLRNRRALILLAQMRRISLFSCLKDRHDFEFPQEEFDGNQFQKAPAISVLHEVIQQTFNLFSTKDSSATWDETLLDKF : 85
SEQ_102 : CDLPQTHSLRNRRALILLAQMGRISLFSCLKDRHDFEFPQEEFDGNQFQKAEAISVLHEVIQQTFNLFSTKDSSAAWDETLLDKF : 85
SEQ_103 : CDLPQTHSLGNRRALILLGQMGRISPFSCLKDRHDFRIPQEVFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_104 : CDLPQTHSLGHRRTMMLLAQMGRISPFSCLKDRHDFRIPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_105 : CDLPQTHSLSNRRTLILLAQMGRISLFSCLKDRHDFEFPQEEFDDNQFQKAQAISVLHEMIQQTFNLFSTKDSSAAWEQSLLDKF : 85
SEQ_106 : CDLPQTHSLRNRRALMLLAQMRRISLFSCLKDRHDFGFPEEEFDGHQFQKAQAISVLHEMIQQTFNLFSTKDSSAAWDETLLDKF : 85
SEQ_107 : CDLPQTHSLRNRRALILLAQMGRISLFSCLKDRHDFGFPQEEFDGNQFQKTQAISVLHEMIQQTFNLFSTEDSSAAWDETLLEKF : 85
SEQ_108 : CDLPQTHSLSNRRTLILLAQMGRISLFSCLKDRHDFEFPQEEFDGNQFQKAEAISVLHEVIQQTFNLFSTKDSSAAWDETLLDKF : 85
SEQ_109 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFRIPQEEFDGNQFQKAQAISVLHEMVQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_110 : CDLPQTHSLGNRRALILLAQMGRISLFSCLKDRHDFEFPQEEFDGNQFQKTQAISVLHEMIQQTFNLFSTKDPSAAWDETLLEKF : 85
SEQ_111 : CDLPQTHSLGHRRTMMLLAQMRRISLFSCLKDRHDFEFPQEEFDGHQFQKTQAVSVLHEMIQQTFNLFSTKDSSATWEQSLLEKF : 85
SEQ_112 : CDLPQTHSLGNRRALILLGQMGRISPFSCLKDRHDFRIPQEVFDGNQFQKAQAISVLHEMIQQTFNLFSTKDSSAAWEQSLLEKF : 85
SEQ_113 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFRIPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_114 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRQDFGFPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSATWEQSLLEKF : 85
SEQ_115 : CDLPQTHSLGHRRTLILLAQMRRISPFSCLKDRHDFGLPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTKDSSDTWDETLLDKF : 85
SEQ_116 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFRIPQEEFDGNQFQKAQAISVLHEMVQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_117 : CDLPQTHSLGNRRALILLAQMGRISLFSCLKDRHDFRFPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_118 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFRIPQEEFDGNQFQKAQAISVLHEVIQQTFNLFSTKDSSAAWDETLLDKF : 85
SEQ_119 : CDLPQTHSLGNRRTLILLAQMGRISLFSCLKDRHDFGFPQGEFDGNQFQKAQAISVLHEMMQQTFNLFSTKHSSATWDETLLDKF : 85
SEQ_120 : CDLPQTHSLGNRRALILLGQMGRISPFSCLKDRHDFRIPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
```

Fig. 6D

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                  *        20         *        40         *        60         *        80
SEQ_121 : CDLPQTHSLGHRRTLMLLAQMRRISLFSCLKDRHDFGFPEEEFDGHQFQKAQAISVLHEVMQQTFNLFSTKNSSAAWEQSLLDKF : 85
SEQ_122 : CDLPQTHSLGHRRTMMLLAQMRRISLFSCLKDRHDFRFPQEEFDGHQFQKAQAISVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_123 : CDLPQTHSLGNRRTMMLLAQMRRISLFSCLKDRHDFGFPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTKDSSDTWDATLLDKF : 85
SEQ_124 : CDLPQTHSLGNRRALILLGQMGRISPFSCLKDRHDFRIPQEVFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_125 : CDLPQTHSLGNRRALILLGQMRRISLFSCLKDRHDFRIPREEFDGNQFQKAEAISVLHEVIQQTFNLFSTKDSSATWEQSLLEKF : 85
SEQ_126 : CDLPQTHSLNNRRTLMLMAQMRRISLFSCLKDRHDFGFPQEEFDGNQFQKAQAISVLHEMMQQTFNLFSTKDSSATWDETLLDKF : 85
SEQ_127 : CDLPQTHSLGHRRTMMLLAQMRRISLFSCLKDRHDFRIPQEVFDGNQFQKAQAISVLHEMIQQTFNLFSTKDSSAAWDETLLDKF : 85
SEQ_128 : CDLPQTHSLGNRRALILLGQMGRISPFSCLKDRHDFRIPQEVFDGNQFQKAQAISVLHEMIQQTFNLFSTKDSSAAWEQSLLEKF : 85
SEQ_129 : CDLPQTHSLRNRRALILLGQMGRISPFSCLKDRHDFRIPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSAAWEQSLLDKF : 85
SEQ_130 : CDLPQTHSLGHRRTMMLLAQMGRISPFSCLKDRHDFRIPQEEFDGNQFQKAQAISVLHEMMQQTFNLFSTEDSSAAWDETLLDKF : 85
SEQ_131 : CDLPQTHSLSNRRTLILLAQMGRISLFSCLKDRHDFEFPQEEFDGNQFQKAQAISVLHEMMQQTFNLFSTKHSSATWDETLLDKF : 85
SEQ_132 : CDLPQTHSLSNRRTLILLAQMGRISLFSCLKDRHDFEFPQEEFG-NQFQKAETIPVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 84
SEQ_133 : CDLPQTHSLGHRRTMMLLAQMGRISLFSCLKDRHDFGFPEEEFDGNQFQKAQAISVLHELIQQTFNLFSTKNSSAAWDETLLDKF : 85
SEQ_134 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFRIPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_135 : CDLPQTHSLGHRRTMMLLAQMRRISLFSCLKDRHDFRFPQEEFDGNQFQKAEAISVLHEMIQQTFNLFSTKDSSDTWDATLLDEF : 85
SEQ_136 : CDLPQTHSLGNRRTMMLLAQMRRISLFSCLKDRHDFGFPQEEFDGNQFQKAQAISVLHEVIQQTFNLFSTKDSSAAWDETLLDKF : 85
SEQ_137 : CDLPQTHSLGNRRTMMLLAQMRRISLFSCLKDRHDFGFPQEEFDGNQFQKAQAISVLHEVIQQTFNLFSTKDSSAAWDETLLDKF : 85
SEQ_138 : CDLPQTHSLGNRRALILLGQMGRISPFSCLKDRHDFRIPEEEFDGHQFQKTQAISVLHEMIQQTFNLFSTKDSSDTWEQSLLEKF : 85
SEQ_139 : CDLPQTHSLSNRRTLILLAQMGRISLFSCLKDRHDFEFPQEEFDDNQFQKAQAISVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_140 : CDLPQTHSLSNRRTLILLAQMGRISLFSCLKDRHDFRIPQEEFDGNQFQKAEAISVLHEMIQQTFNLFSTKDSSATWDATLLDKF : 85
SEQ_141 : CDLPQTHSLGNRRAMMLLAQMRRISLFSCLKDRHDFEFPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTKDSSATWDATLLDKF : 85
SEQ_142 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRYDFRIPQEEFDGNQFQKTQAISVLHEMIQQTFNLFSTKDSSAAWDETLLDEF : 85
SEQ_143 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFRIPQEVFDGNQFQKAQAISVLHEVIQQTFNLFSTKDSSAAWDETLLDKF : 85
SEQ_144 : CDLPQTHSLRNRRALILLAQMGRISLFSCLKDRHDFGFPQEEFDGNQFQKTQAISVLHEMIQQTFNLFSTEDSSATWDETLLDKF : 85
SEQ_145 : CDLPQTHSLGNRRALILLGQMGRISPFSCLKDRHDFRIPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_146 : CDLPQTHSLSNRRTLILLAQMGRISLFSCLKDRHDFEFPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTKDSSATWDATLLDKF : 85
SEQ_147 : CDLPQTHSLGHRRTMMLLAQMRRISLFSCLKDRHDFEFPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSATWEQSLLEKF : 85
SEQ_148 : CDLPQTHSLRNRRALILLAQMGRISLFSCLKDRHDFGLPQEEFDGHQFQKAEAISVLHEVIQQTFNLFSTEDSSAAWEQSLLDKF : 85
SEQ_149 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFRIPQEEFDGNQFQKAQAISVLHEMVQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_150 : CDLPQTHSLGNRRTLILLAQMGRISLFSCLKDRHDFRFPQEEFDGNQFQKAEAISVLHEVIQQTFNLFSTKDSSAAWDETLLDKF : 85
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Fig. 6E

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                  *        20         *        40         *        60         *        80
SEQ_151 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFRIPQEVFDGNQFQKAEAISVLHEMVQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_152 : CDLPQTHSLGNRRALILLAQMRRISLFSCLKDRHDFEFPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTKDSSATWDETLLDKF : 85
SEQ_153 : CDLPQTHSLGNRRTMMLLAQMRRISLFSCLKDRHDFGFPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTKNSSAAWDEDLLDKF : 85
SEQ_154 : CDLPQTHSLRNRRALILLAQMRRISLFSCLKDRHDFRLPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTKDSSDTWDATLLDKF : 85
SEQ_155 : CDLPQTHSLGHRRTMMLLAQMRRISLFSCLKDRHDFGFPQEEFDGNQFQKTQAISVLHEMIQQTFNLFSTKDSSDTWDATLLDKF : 85
SEQ_156 : CDLPQTHSLGNRRALMLLAQMRRISLFSCLKDRQDFGFPEEEFDGNQFQKAQAISVLHEMMQQTFNLFSTKNSSAAWDETLLEKF : 85
SEQ_157 : CDLPQTHSLRNRRALILLAQMGRISLFSCLKDRHDFRIPQEEFDGHQFQKAQAISVLHELIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_158 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFRIPQEEFDGNQFQKTQAISVLHGMIQQTFNLFSTKDSSAAWDEDLLDKF : 85
SEQ_159 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFRIPREEFDGNQFQKAEAISVLHEVIQQTFNLFSTKDSSAAWDEDLLDKF : 85
SEQ_160 : CDLPQTHSLGHRRTMMLLAQMGRISLFSCLKDRHDFEFPQEEFDGNQFQKTQAISVLHEMIQQTFNLFSTEDSSAAWDETLLDKF : 85
SEQ_161 : CDLPQTHSLGNRRALILLAQMRRISLFSCLKDRHDFGFPQEEFDGNQFQKTQAISVLHEMIQQTFNLFSTKDSSAAWEQSLLEKF : 85
SEQ_162 : CDLPQTHSLGNRRALILLAQMRRISLFSCLKDRHDFRFPQEEFDGNQFQMTQAISVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_163 : CDLPQTHSLGNRRALILLAQMGRISLFSCLKDRHDFGFPEGEFDGNQFQKAQAISVLHEMIQQTFNLFSTEGSSAAWEQSLLEKF : 85
SEQ_164 : CDLPQTHSLDNRRTLMLLAQMRRISLFSCLKDRHDFRIPQEVFDGNQFQKAETIPVLHEMIQQIFNLFSTEDSSAAWEQSLLDKF : 85
SEQ_165 : CDLPQTHSLGSRRTLMLLAQMRRISLFSCLKDRHDFGLPQEEFDGNQFQKAQAISVLHEVIQQTFNLFSTKDSSAAWDETLLDKF : 85
SEQ_166 : CDLPQTHSLGNRRVLILLAQMRRISLFSCLKDRHDFGFPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTKNSSAAWDEDLLDKF : 85
SEQ_167 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFRIPREEFDGNQFQKAEAISVLHEVIQQTFNLFSTKDSSAAWDEDLLDKF : 85
SEQ_168 : CDLPQTHSLGNRRALILLAQMRRISLFSCLKDRYDFRIPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTKDSSVAWDERLLDKL : 85
SEQ_169 : CDLPQTHSLGNRRALILLAQMGRISLFSCLKDRHDFGFPEGEFDGNQFQKAQAISVLHEMIQQTFNLFSTEDLSAAWEQSLLEKF : 85
SEQ_170 : CDLPQTHSLGNRRALILLAQMGRISLFSCLKDRHDFGLPQEEFDGNQFQKAEAISVLHEVIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_171 : CDLPQTHSLGNRRALILLAQMGRISLFSCLKDRHDFGFPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSAAWDETLLEKF : 85
SEQ_172 : CDLPQTHSLNNRRTLMLMAQMRRISLFSCLKDRHDFEFPQEEFDGNQFQKAQAISVLHELIQQTFNLFSTKDSSDTWDETLLDKF : 85
SEQ_173 : CDLPQTHSLGSRRTLMLLAQMRRISLFSCLKDRHDFGFPEEEFDGNQFQKAQAISVLHEMMQQTFNLFSTKNSSAAWDETLLEKF : 85
SEQ_174 : CDLPQTHSLGHRRTMMLLAQMGRISLFSCLKDRHDFGFPEEEFDGHQFQKAQAISVLHEVMQQTFNLFSTEDSSAAWDETLLDKF : 85
SEQ_175 : CDLPQTHSLDNRRTLMLLAQMRRISLFSCLKDRHDFGFPQEEFDGNQFQKAQAISAFHEMIQQTFNLFSTKDSSDTWDATLLDKF : 85
SEQ_176 : CDLPQTHSLDNRRTLMLLAQMRRISLFSCLKDRHDFRIPQEVFDGNQFQKAEAISVLHEVIQQTFNLFSTKDSSAAWDETLLDKF : 85
SEQ_177 : CDLPQTHSLGHRRTMMLLAQMRRISLFSCLKDRHDFGFPQEEFDDNQFQKAQAISVLHEMMQQTFNLFSTEDSSDTWDETLLEKF : 85
SEQ_178 : CDLPQTHSLGNRRALILLAQMGRISLFSCLKDRHDFRFPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTKDSSAAWDETLLEKF : 85
SEQ_179 : CDLPQTHSLDNRRTLMLMAQMGRISLFSCLKDRHDFRFPQEVFDGNQFQKAQAISAFHEMIQQTFNLFSTEDSSAAWDETLLEKF : 85
SEQ_180 : CDLPQTHSLRSRRTLMLLAQMRRISLFSCLKDRHDFGLPQEEFDGNQFQKAQAISVLYEMIQQTFNLFSTEDSSATWEQSLLDKF : 85
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Fig. 6F

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                  *        20         *        40         *        60         *        80
SEQ_181 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFRIPREEFDGNQFQKAEAISVLHEVIQQTFNLFSTKNSSAAWDEDLLDKF : 85
SEQ_182 : CDLPQTHSLNNRRTLMLMAQMRRISLFSCLKDRHDFGFPQEEFDDNQFQKAQAISVLHEMMQQTFNLFSTEDSSAAWDETLLEKF : 85
SEQ_183 : CDLPQTHSLRNRRALILLAQMGRISLFSCLKDRYDFGFPQEEFDGHQFQKTQAISVLHELMQQTFNLFSTKDSSAAWEQSLLEKF : 85
SEQ_184 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFGLPQEEFDGNQFQKAQAISVLHEMVQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_185 : CDLPQTHSLGNRRALILLAQMGRISLFSCLKDRHDFGLPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTKDSSDTWDATLLDKF : 85
SEQ_186 : CDLPQTHSLGNRRALILLAQMGRISLFSCLKDRHDFGFPEGEFDGHQFQKTQAISVLHEMMQQTFNLFSTKDSSATWDETLLDKF : 85
SEQ_187 : CDLPQTHSLSNRRTLMIMAQMGRISPFSCLKDRHDFGLPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_188 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFGFPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_189 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFGLPQEEFDGNQFQKTQAISVLHEMMQQTFNLFSTKNSSDTWDATLLDKF : 85
SEQ_190 : CDLPQTHSLGNRRALILLGQMGRISPFSCLKDRHDFRIPQEVFDGNQFQKAQAISVLHEMIQQTFNLFSTKDSSAAWEQSLLEKF : 85
SEQ_191 : CDLPQTHSLGHRRTMMLLAQMGRISLFTCLKDRHDFGFPQEEFDGNQFQKAQAISVLHELFQQTFNLFTTKDSSAAWDETLLDKF : 85
SEQ_192 : CDLPQTHSLGHRRTMILLAQMGRISPFSCLKDRHDFRIPQEEFDGNQFQKAQAISVLHEVIQQTFNLFSTKDSSAAWDETLLDKF : 85
SEQ_193 : CDLPQTHSLRNRRALILLGQMGRISPFSCLKDRHDFRIPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTKDSSAAWDETLLEKF : 85
SEQ_194 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFGFPQEEFDGNQFQKTQAISVLHELIQQTFNLFSTKDSSATWDETLLDKF : 85
SEQ_195 : CDLPQTHSLSNRRTLILLAQMGRISLFSCLKDRHDFEFPQEEFDDNQFQKAQAISVLHEVIQQTFNLFSTKDSSAAWDETLLDKF : 85
SEQ_196 : CDLPQTHSLGHRRTMMLLAQMGRISPFSCLKDRHDFGFPQEEFDGHQFQKAQAISVLHELIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_197 : CDLPQTHSLGHRRTMMLLAQMGRISLFSCLKDRHDFRFPQEEFDGNQFQKAQAISVLHEMMQQTFNLFSTKHSSATWDETLLDKF : 85
SEQ_198 : CDLPQTHSLGSRRTLMLLAQMRRISLFSCLKDRHDFGFPEEEFDGNQFQKAQAISVLHEMMQQTFNLFSTKNSSAAWDETLLEKF : 85
SEQ_199 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFRIPQEEFDGNQFQKAQAISVLHEMVQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_200 : CDLPQTHSLGNRRALILLAQMRRISLFSCLKDRHDFRFPQEEFDGNQFQKAEAISVLHEVIQQTFNLFSTKNSSAAWDEDLLDKF : 85
SEQ_201 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFGLPQEEFDGNQFQKTQAISVLHEVIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_202 : CDLPQTHSLGNRRALILLAQMGRISLFSCLKDRHDFRFPQEEFDGNQFQKAQAISAFHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_203 : CDLPQTHSLGHRRTMMLLAQMRRISLFSCLKDRHDFGLPQEEFDGHQFQKTQAISVLHEMMRQTFNLFSTKDSSDTWDATLLDKF : 85
SEQ_204 : CDLPQTHSLGNRRALILLAQMGRISLFSCLKDRHDFGLPQEEFDGNQFQKAEAISVLHEMIQQTFNLFSTEDSSAAWEQSLLDKF : 85
SEQ_205 : CDLPQTHSLGNRRAFILLAQMGRISPFSCLKDRHDFGFPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTKNSSAAWDEDLLDKF : 85
SEQ_206 : CDLPQTHSLRNRRALILLAQMGRISLFSCLKDRHDFGFPQEEFDGNQFQKAEAISVLHEVIQQTFNLFSTEDSSATWEQSLLEKF : 85
SEQ_207 : CDLPQTHSLGNRRALILLAQMRRISLFSCLKDRHDFGLPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSAAWEQSPLEKF : 85
SEQ_208 : CDLPQTHSLGNRRALMLLAQMRRISLFSCLKDRHDFEFPQEEFDGNQFQKAEAISVLHEMIQQTFNLFSTEDSSAAWDEDLLDKF : 85
SEQ_209 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFRIPREEFDGNQFQKAEAISVLHEVIQQTFNLFSTKDSSAAWDETLLDKF : 85
SEQ_210 : CDLPQTHSLGHRRTMMLLAQMRRISLFSCLKDRHDFGFPQEEFDGNQFQKAQAISAFHEMIQQTFNLFSTEDSSAAWDETLLEKF : 85
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Fig. 6G

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                   *         20         *         40         *         60         *         80
SEQ_211 : CDLPQTHSLGHRRALILLAQMGRISLFSCLKDRHDFEFPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTKDSSATWDETLLDKF : 85
SEQ_212 : CDLPQTHSLGNRRALILLAQMRRISLFSCLKDRHDFRIPQEVFDGNQFQKAETIPVLHEVIQRTFNLFSTKDSSAAWDETLLDKF : 85
SEQ_213 : CDLPQTHSLGNRRALILLAQMRRISPFSCLKDRHDFRFPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTKDSSAAWEQSLLEKF : 85
SEQ_214 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFGFPQEEFDGNQFQKAQAISVLHEMMQQTFNLFSTKNSSAAWDETLLEKF : 85
SEQ_215 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFRIPREEFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSATWEQSLLEKF : 85
SEQ_216 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFGFPEEEFDGHQFQKTQAISVLHEMIQQTFNLFSTKDSSAAWDERLLEKF : 85
SEQ_217 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFGFPQEEFDGNQFQKAPAISVLHEVIQQTFNLFSTKDSSAAWDETLLDEF : 85
SEQ_218 : CDLPQTHSLGNRRALILLAQMGRISLFSCLKDRHDFGLPQEEFDGNQFQKTQAISVLHEMMQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_219 : CDLPQTHSLNNRRTLMLMAQMRRISLFSCLKDRHDFGFPEEEFDGHQFQKTQAISVLHEVIQQTFNLFSTKDSSAAWDETLLDEF : 85
SEQ_220 : CDLPQTHSLGNRRALILLAQMRRISPFSCLKDRHDFGFPQEEFDGNQFQKAPAISVLHEVIQQTFNLFSTKDSSAAWDETLLDEF : 85
SEQ_221 : CDLPQTHSLGNRRALILLAQMRRISPFSCLKDRHDFGLPQEEFDGNQFQKAQAISVLHEVIQQTFNLFSTKDSSAAWDETLLDEF : 85
SEQ_222 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFGFPEEEFDGHQFQKAQAISVLHEMIQQTFNLFSTEDSSAAWDETLLEKF : 85
SEQ_223 : CDLPQTHSLGNRRALILLAQMGRISLFSCLKDRHDFRFPQEEFDGNQFQKAQAISVLHEMVQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_224 : CDLPQTHSLGHRRTLMLLAQMRRISLFSCLKDRHDFGFPEEEFDGHQFQKAPAISVLHEVIQQTFNLFSTKDSSAAWDETLLDEF : 85
SEQ_225 : CDLPQTHSLNNRRTLMLMAQMRRISPFSCLKDRYDFGFPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSAAWDETLLEKF : 85
SEQ_226 : CDLPQTHSLGNRRALILLAQMRRISPFSCLKDRHDFGFPQEEFDGNQFQKAQAISVLLEMIQQTFNLFSTKDSSAAWDETLLDKF : 85
SEQ_227 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFGFPQEEFDGNQFQKAPAISVLHEVIQQTFNLFSTKDSSAAWDEDLLDKF : 85
SEQ_228 : CDLPQTHSLGNRRALILLTQMRRISPFSCLKDRHDFEFPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSAAWDETLLEKF : 85
SEQ_229 : CDLPQTHSLGNRRALILLGQMGRISPFSCLKDRHDFRIPQEVFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSATWEQSLLEKF : 85
SEQ_230 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFGFPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTKNSSAAWDEDLLDKF : 85
SEQ_231 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFRIPREEFDGNQFQKAEAISVLHEVIQQTFNLFSTKDSSAAWDETLLDEF : 85
SEQ_232 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFRIPREEFDGNQFQKAEAISVLHEVIQQTFNLFSTKDSSAAWDETLLEKF : 85
SEQ_233 : CDLPQTHSLGHRRTMMLLAQMRRISLFSCLKDRHDFGFPEEEFDGHQFQKTQAISVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_234 : CDLPQTHSLSNRRTLILLAQMGRISLFSCLKDRHDFEFPQEEFDDNQFQKAQAISVLHEMIQQTFNLFSTKDSSAAWEQSLLDKF : 85
SEQ_235 : CDLPQTHSLGNRRALILLAQMRRISPFSCLKDRHDFGLPQEEFDGDQFQKTQAISVLHEMIQQTFNLFSTKDSSDTWDATLLDEF : 85
SEQ_236 : CDLPQTHSLGHRRTMMLLAQMRRISPFSCLKDRHDFGLPQEVFDGNQFQKAQAISAFHEMIQQTFNLFSTEDSSATWEQSLLEKF : 85
SEQ_237 : CDLPQTHSLGNRRALILLAQMGRISLFSCLKDRHDFGFPEEEFDGHQFQKTQAISVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_238 : CDLPQTHSLGNRRALILLAQMGRISLFSCLKDRHDFRFPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTKNSSAAWDETLLDEF : 85
SEQ_239 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFGFPEEEFDGHQFQKTQAISVLHEMIQQTFNLFSTKDSSAAWDERLLEKF : 85
SEQ_240 : CDLPQTHSLGNRRALILLAQMGRISLFSCLKDRHDFRFPQEEFDGNQFQKAPAISVLHEVIQQTFNLFSTKDSSAAWDETLLDEF : 85
```

Fig. 6H

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                    *        20         *        40         *        60         *        80
SEQ_241 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFGFPEEEFDGHQFQKTQAISVLHEMIQQTFNLFSTKDSSAAWDERLLEKF : 85
SEQ_242 : CDLPQTHSLGNRRALILLAQMGRIPLFSCLKDRHDFRFPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTKDSSATWDETLLDKF : 85
SEQ_243 : CDLPQTHSLGNRRALVLLAQMGRISPFSCLKDRHDFGFPEEEFDGHQFQKTQAISVLHEMIQQTFNLFNTKDSSAAWDERLLEKF : 85
SEQ_244 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFRIPQEEFDGNQFQKAQAISVLHEMVQQTFNLFNTEDSSAAWEQSLLEKF : 85
SEQ_245 : CDLPQTHSLGHRRTMMLLAQMGRISPFSCLKDRHDFRIPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSATWEQSLLEKF : 85
SEQ_246 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRYDFEFPQEEFDGHQFQKAQAISVLHEMMQQTFNLFSTKDSSAALDETLLDEF : 85
SEQ_247 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFRIPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_248 : CDLPQTHSLGNRRTMMLLAQMRRISLFSCLKDRHDFGFPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTKNSSAAWDETLLEKF : 85
SEQ_249 : CDLPQTHSLGHRRTMMLLAQMRRISLFSCLKDRHDFGFPEEEFDGHQFQKTQAISVHHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_250 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFGFPEEEFDGHQFQKTQAISVLHEMIQQTFNLFSTKDSSAAWDERLLEKF : 85
SEQ_251 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFGFPEEEFDGNQFQKAQAISVLHEVIQQTFNLFSTKDSSAALDETLLEKF : 85
SEQ_252 : CDLPQTHSLGNRRALILLAQMGRISLFSCLKDRHDFEFPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTKDSSATWDATLLDKF : 85
SEQ_253 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFGLPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTKNSSAAWDETLLEKF : 85
SEQ_254 : CDLPQTHSLGHRRTMMLLAQMRRISLFSCLKDRHDFRFPQEEFDGNQFQKTQAISVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_255 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFGFPQEEFDGHQFQKAQAISVLHELIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_256 : CDLPQTHSLGNRRALILLAQMRRISPFSCLKDRHEFRFPEEEFDSNQFQKAQAISVLHEMIQQTFNLFSTKDSSDTWDATLLDEF : 85
SEQ_257 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFEFPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_258 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFEFPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTKDSSDTWDATLLDKF : 85
SEQ_259 : CDLPQTHSLGHRRTMMLLAQMRRISLFSCLKDRHDFRFPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTKDSSATWEQSLLEKF : 85
SEQ_260 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFGLPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_261 : CDLPQTHSLGHRRTMMLLAQMGRISPFSCLKDRHDFRIPQEEFDGNQFQKAQAISVLHEMMQQTFNLFSTKHSSATWDETLLDKF : 85
SEQ_262 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFGLPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTKDSSAAWDERLLEKF : 85
SEQ_263 : CDLPQTHSLDNRRTLMLLAQMGRISLFSCLKDRHDFGFPEEEFD-KQFQKAQAISVLHEMIQQTFNLFSTKNSSAAWDEDLLDKF : 84
SEQ_264 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFGFPEEEFDGHQFQKTQAISVLHEMIQQTFNLFSTKDSSAAWDERLLEKF : 85
SEQ_265 : CDLPQTHSLSNRRTLILLAQMGRISPFSCLKDRHDFRIPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_266 : CDLPQTHSLGNRRALILLAQMGRISLFSCLKDRHDFRFPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSATWEQSLLEKF : 85
SEQ_267 : CDLPQTHSLGNRRALMLLAQMRRISLFSCLKDRHDFGLPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTKDSSATWDETLLDKF : 85
SEQ_268 : CDLPQTHSLGNRRTMMLLAQMRRISLFSCLKDRHDFRFPQEVFDGNQFQKAQAISVLHEMIQQTFNLFSTKDSSATWDETLLDKF : 85
SEQ_269 : CDLPQTHSLGSRRTLMLLAQMRRISLFSCLKDRHDFRFPQEEFDGNQFQKAQAISVLHEMMQQTFNLFSTKDSSDTWDVTLLDKF : 85
SEQ_270 : CDLPQTHSLRNRRALILLAQMRRISLFSCLKDRHDFGLPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTKDSSATWEQSLLEKF : 85
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Fig. 6I

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                     *        20         *        40         *        60         *        80
SEQ_271 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFRIPREEFDGNQFQKAEAISVLHEVIQQTFNLFSTKDSSAAWDETLLDKF : 85
SEQ_272 : CDLPQTHSLSNRRTLILLAQMGRISLFSCLKDRHDFRIPQEEFDGNQFQKAQAISVLHEMMQQTFNLFSTKHSSATWDETLLDKF : 85
SEQ_273 : CDLPQTHSLRNRRALILLAQMGRISLFSCLKDRHDFGFPEEEFDGHQFQKAQAISVLHEVMQQTFNLFSTKNSSAAWEQSLLEKF : 85
SEQ_274 : CDLPQTHSLGNRRALILLAQMRRISLFSCLKDRHDFGFPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSATWEQSLLEKF : 85
SEQ_275 : CDLPQTHSLGNRRALILLAQMGRISLFSCLKDRHDFEFPQEEFDGNQFQKTQAISAFHEMIQQTFNLFSTKDSSDTWDATLLDKF : 85
SEQ_276 : CDLPQTHSLGNRRALILLGQMGRISPFSCLKDRHDFRIPQEVFDGNQFQKAQAISVLHEMIQQTFNLFSTKDSSAAWEQSLLEKF : 85
SEQ_277 : CDLPQTHSLGHRRTMMLLAQMRRISPFSCLKDRHDFRIPQEVFDGNQFQKAQAISVLHEMIQQTFNLFSTKDSSAAWEQSLLEKF : 85
SEQ_278 : CDLPQTHSLSNRRTLILLAQMGRISLFSCLKDRHDFEFPQEEFDDNQFQKAQAISVLHEMIQQTFNLFSTKDSSAAWDETLLDKF : 85
SEQ_279 : CDLPQTHSLGHRRTMMLLAQMRRISLFSCLKDRHDFRIPQEEFDGNQFQKAQAISVLHEVIQQTFNLFSTKDSSATWEQSLLEKF : 85
SEQ_280 : CDLPQTHSLGHRRTLMLLAQMRRISLFSCLKDRHDFGFPEEEFDGHQFQKAQAISVLHEVMQQTFNLFSTKHSSATWDETLLDKF : 85
SEQ_281 : CDLPQTHSLGHRRTMMLLAQMRRISLFSCLKDRHDFRFPQEEFDGNQFQKAEAISVLHEVIQQTSNLFSTKDSSAAWEQSLLEKF : 85
SEQ_282 : CDLPQTHSLGHRRTMMLLAQMRRISLFSCLKDRHDFGFPEEEFDGHQFQKAQAISVLHEVMQQTFNLFSTKNSSAAWEQSLLEKF : 85
SEQ_283 : CDLPQTHSLGNRRAFILLAQMGRISPFSCLKDRHDFRIPQEVFDGNQFQKAQAISVLHEMIQQTFNLFSTKDSSAAWEQSLLEKF : 85
SEQ_284 : CDLPQTHSLGNRRALILLAQMRRISLFSCLKDRHDFGLPQEEFDGNQFQKTQAISVLHEMIQQTFNLFSTKDSSAAWEQSLLEKF : 85
SEQ_285 : CDLPQTHSLNNRRTLMLMAQMGRISLFSCLKDRHDFEFPQEEFDDNQFQKAQAISVLHEMIQQTFNLFSTKDSSAAWEQSLLDKF : 85
SEQ_286 : CDLPQTHSLGNRRALILLAQMGRISPSSCLKDRHDFGFPEEEFDGNQFQKAPAISAFHEMIHQTFNLFSTEDSSAAWDETLLDKF : 85
SEQ_287 : CDLPQTHSLSHRRTLMLLAQMRRISPFSCLKDRHDFGFPREEFDGNQFQKAQAISVLHEVIQQTFNLFSTKDSSDAWDATLLDKF : 85
SEQ_288 : CDLPQTHSLRNRRALILLAQMGRISLFSCLKDRHDFEFPQEEFDGNQFQKTQAISVLHEMIQQTFNLFSTKDSSAAWEQSLLEKF : 85
SEQ_289 : CDLPQTHSLGHRRTMMLLAQMGRISLFSCLKDRHDFRFPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_290 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFGLPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_291 : CDLPQTHSLGNRRALILLAQMGRISLFSCLKDRHDFRFPQEEFDGHQFQKAQAISVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_292 : CDLPQTHSLGNRRALILLAQMGRISLFSCLKDRHDFGFPEEEFDGNQFQKAQAISVLHEVIQQTFNLFSTKHSSATWDETLLDKF : 85
SEQ_293 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFGFPQEEFDGNQFQKAQAISVLHELIQQTFNLFSTKNSSAALDETLLDEF : 85
SEQ_294 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFGFPQEEFDGNQFQKAPAISVLHEVIQQTFNLFSTKDSSAAWDETLLDEF : 85
SEQ_295 : CDLPQTHSLGNRRALILLGQMGRISPFSCLKDRHDFRIPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_296 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFRIPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_297 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFGFPEEEFDGHQFQKTQAISVLHEMIQQTFNLFSTKDSSAAWDERLLEKF : 85
SEQ_298 : CDLPQTHSLGNRRALILLAQMGRISLFSCLKDRHDFGFPEEEFDGNQFQKAEAISVLHEVIQQTFNLFSTKDSSAAWDETLLDKF : 85
SEQ_299 : CDLPQTHSLGHRRTMMLLAQMGRISPFSCLKDRHDFRIPQEEFDGNQFQKAQAISVLHEMMQQTFNLFSTKHSSATWDETLLDKF : 85
SEQ_300 : CDLPQTHSLRNRRALILLAQMGRISLFSCLKDRHDFGFPQEEFDGNQFQKTQAISVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
```

Fig. 6J

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                    *        20         *        40         *        60         *        80
SEQ_301 : CDLPQTHSLGNRRALILLAQMGRISLFSCLKDRHDFEFPQEEFDGNQFQKTQAISVLHEMIQQTFNLFSTKDPSAAWDETLLEKF : 85
SEQ_302 : CDLPQTHSLGHRRTMMLLAQMRRISPFSCLKDRHDFGLPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_303 : CDLPQTHSLGNRRALILLAQMRRISPFSCLKDRHEFRFPEEEFDSNQFQKAQAISVLHEMIQQTFNLFSTKDSSDTWDATLLDEF : 85
SEQ_304 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFGFPEEEFDGHQFQKTQAISVLHEMIQQTFNLFSTKDSSAAWDERLLEKF : 85
SEQ_305 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFGFPQEEFDGNQFQKAPAISVLHEVIQQTFNLFSTKDSSAAWDETLLDEF : 85
SEQ_306 : CDLPQTHSLGNRRAFILLAQMGRISPFSCLKDRHDFGFPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTKNSSAAWDEDLLDKF : 85
SEQ_307 : CDLPQTHSLDNRRTLMLLAQMRRISLFSCLKDRHDFGFPQEEFDGNQFQKAQAISAFHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_308 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFGFPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTKNSSAAWDEDLLDKF : 85
SEQ_309 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFRIPQEEFDGNQFQKAQAISVLHEMVQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_310 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFGFPEEEFDGHQFQKTQAISVLHEMIQQTFNLFSTKDSSAAWDERLLEKF : 85
SEQ_311 : CDLPQTHSLGHRRTMMLLAQMRRISLFSCLKDRHDFGFPEEEFDGHQFQKTQAISVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_312 : CDLPQTHSLGNRRALILLAQMGRISPFSCLKDRHDFGFPEEEFDGHQFQKTQAISVLHEMIQQTFNLFSTKDSSAAWDERLLEKF : 85
SEQ_313 : CDLPQTHSLRNRRALILLAQMGRISHFSCLKDRYDFGFPQEEFDGHQFQKTQAISVLHEMIQQTFNLFSTEDSSAAWDETLLDEF : 85
SEQ_314 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFRIPQEEFDGNQFQKAPAISVLHEMIQQTFNLFSTEDSSAAWEQSLLEKF : 85
SEQ_315 : CDLPQTHSLRNRRALILLAQMGRISPFSCLKDRHDFRIPREEFDGNQFQKAEAISVLHEVIQQTFNLFSTKNSSAAWDEDLLDKF : 85
SEQ_316 : CDLPQTHSLGNRRTMMLLAQMRRISLFSCLKDRHDFGFPQEEFDGNQFQKAQAISVLHEMIQQTFNLFSTKDSSATWEQSLLEKF : 85
SEQ_317 : CDLPQTHSLGHRRTLMLLAQMRRISLFSCLKDRHDFGFPEEEFDGHQFQKAQAISVLHEVMQQTFNLFSTKNSSAAWEQSLLEKF : 85
SEQ_318 : CDLPQTHSLGHRRTLMLLAQMRRISLFSCLKDRHDFGFPEEEFDGHQFQKAQAISVLHEVMQQTFNLFSTKNSSAAWEQSLLEKF : 85
SEQ_319 : CDLPQTHSLGNRRALILLAQMGRISLFSCLKDRHDFRFPQEEFDGNQFQKAQAISVLHEMMQQTFNLFSTKHSSATWDETLLDKF : 85
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Fig. 6K

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                  *        100         *        120         *        140         *        160
SEQ_001 : STELYRQLNDLEACVIQEVGVEETPLMNADSILPVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_002 : YIELDQQLNDLEACVMQEVWVGGTPLMNEDSILAVKKYFQRITLYLMEKKYSSCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_003 : STELYRQLNDLEACVIQEVGVEETPLMNEDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_004 : YIELDQQLNDLEACVMQEVWVGGTPLMNVDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_005 : YIELDQQLNDLEACMIQEVGVEETPLMNVDSILAVKKYFQRITLYLVGKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_006 : YIELDQQLNDLEACVMQEVWVGGTPLMNEDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_007 : YVELDQQLNDLEACVIQEVGVEEIALMNEDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_008 : YIELDQQLNDLEACVMQEVWVGGTPLMNEDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_009 : YIELDQQLNDLESCVMQEVGVIESPLMNEDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_010 : YIELDQQLNDLEACMIQEVGVEETPLMNVDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_011 : YIELDQQLNDLEACVMQEVWVGGTPLMNEDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_012 : YIELDQQLNDLESCVMQEVGVTGTPLMNEDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_013 : YIELDQQLNDLESCVMQEVGVIESPLMNEDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_014 : YIELDQQLNDLEACVIQEVGVIESPLMNEDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_015 : YIELDQQLNDLEACVILGVGVTETPLMKEDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_016 : YIELDQQLNDLEACVMQEVWVGGTPLMNEDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_017 : YIELDQQLNDLESCVMQEVGVIESPLMNEDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_018 : STELYRQLNDLEACVIQEVGVEETPLMNADSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_019 : YIELDQQLNDLESCVMQEVGVIESPLMKEDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_020 : YIELDQQLNDLEACVILGVGVTETPLMKEDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_021 : YIELDQQLNDLEACVMQEVWVGGTPLMNEDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_022 : YIELDQQLNDLEACVILGVGVTETPLMKEDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_023 : YIELDQQLNDLEACMIQEVGVEETPLMNVDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_024 : YVELDQQLNDLEACVIQEVGVEETPLMNADSILPVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_025 : YVELDQQLNDLEACVIQEVGVEEIALMNEDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_026 : YTELDQQLNDLEACVMQEVWVGGTPLMNEDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_027 : YIELDQQLNDLEACVILGVGVTETPLMKEDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_028 : YIELDQQLNDLEACVIQEVGVEETPLMNEDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_029 : YIELDQQLNDLEACVMQEVWVGGTPLMNEDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_030 : YIELDQQLNDLEACMIQEVGVEETPLMNVDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
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Fig. 6L

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                    *       100         *       120         *       140         *       160
SEQ_031 : YIELDQQLDDLEACMIQEVGVEETPLMNVDSILAVKKYFQRITLYLVGKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_032 : YVELDQQLNDLEACVIQEVGVEETPLMNEDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_033 : YIELDQQLNDLESCVMQEVGVIESPLMNEDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_034 : YIELDHQLNDLEACVTQEVGVEETPLMNVDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_035 : YIELDQQLNDLESCVMQEVGVIESPLMNEDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_036 : YIELDQQLNDLEACVIQEVGVEETPLMNEDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_037 : YVELDQQLNDLEACVIQEVGVEEIALINEDFILAVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_038 : YIELDQQLNDLESCVMQEVGVIESPLMNEDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_039 : YIELDQQLNDLESCVMQEVGVIESPLMNEDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_040 : YIELDQQLNDLEACVILGVGVTETPLMKEDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_041 : YIELDQQLNDLESCVMQEVGVIESPLMNEDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_042 : YIELDQQLNDLEACVMQEVWVGGTPLMNEDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_043 : YIELDQQLNDLEACVIQEVGVEETPLMNEDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_044 : STELYRQLNDLEACVIQEVGVEETPLMNADSILPVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_045 : YIELDQQLNDLESCVMQEVGVIESPLMNEDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_046 : YIELDQQLNDLEACVIQEVGMEETPLMNEDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_047 : YIELDQQLNDLEACMIQEVGVEETPLMNVDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_048 : YIELDQQLNDLEACVMQEVWVGGTPLMNEDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_049 : YIELDQQLNDLEACVMQEVWVGGTPLMNEDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_050 : YIELDQQLNDLESCVMQEVGVIESPLMNEDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_051 : YIELDQQLNDLESCVMQEVGVIESPLMNEDSILAVKKYFQRITLYLTEKKYSPCVWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_052 : YIELFQQLNDLEACVTQEVGVEEIALMNEDSILAVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_053 : YIELNQQLNDLEACVIQEVGVEETALMNVDSILAVKKYFQRITLYLMEKKYSSCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_054 : STELNQQLNDLEACVIQEVGMEETPLMNEDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_055 : CTELYQQLNDLEACVMQEERVGETPLMNADSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_056 : YIELDQQLNDLESCVMQEVGVIESPLMYEDSILAVRKYFQRITLYLTERKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 165
SEQ_057 : STELNQQLNDLEACVIQEVGVEETPLMNEDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_058 : STELYQQLNDLEACVMQEERVGETPLMNADSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_059 : YTELNQQLNDLEACVMQEERVGETPLMNVDSVLAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_060 : YTELNQQLNDLEACVIQEVGVEETPLMNEDSILAVKKYFQRITLYLMEKKYSPCSWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
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Fig. 6M

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                   *        100         *        120         *        140         *        160
SEQ_061 : YIELNQQLNDLEACVIQEVGVEETPLINVDPILAVRKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_062 : YIELNQQLNDLEACVIQEVGVEEIALMNEDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_063 : STELNQQLNDLEACVIQEVGVGETPLMNADSILAVKKYFRRITLYLTEKKYNPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_064 : YTELYQQLNDLEACVIQEVGVEEIALMNEDSILAVRKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 165
SEQ_065 : YIELDQQLNDLEACMIQEVGVEETPLMNVDSILAVKKYFQRITLYLVGKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_066 : STELYQQLNDLEACVMQEERVGETPLMNADSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_067 : YTELYQQLNDLEACVIQEVGVEETPLRNVDSILAVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_068 : YIELFQQLNDLEACVMQEERVGETPLMNVDSILAVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_069 : STELYQQLNDLEACVIQEVGVEETPLMNVDSILAVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_070 : YTELYQQLNDLEACVIQEVGVEEIALMNEGSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_071 : YIELDQQLNDLEACMIQEVGVEETPLMNVDSILAVKKYFQRITLYLVGKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_072 : YTELYQQLNDLEACVIQEVGVEEIALMNEGSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_073 : YIELDQQLNDLESCVMQEVGVIESPLMNEDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_074 : YIELDQQLNDLEACVILGVGVTETPLMKEDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_075 : STELYQQLNDLEACVMQEERVGETPLMNADSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_076 : STELNRQLNDLEACVTQEVGVEETPLMNADSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_077 : YIELDQQLNDLESCVMQEVGVTGTPLMNEDSILAVKKYFQRITLYLTEKKHSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_078 : STELYQQLNDLEACVIQGVGVTETPLMNEDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_079 : YIELFQQLNDLEACMMQKVGVEETPLMNEDSILAVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_080 : YTELNQQLNDLEACVIQEVGVEETPLMNVDSILTVRKYFQRITLYLTEKKYSPCSWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_081 : YIELNQQLNDLEACVIQEVGVEETPLMNEDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_082 : YTELNQQLNDLEACVIQEVGVEETPLMNVDSILAVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_083 : YTELNQQLNDLEACVMQEERVGETPLMNADSILAVKKYFRRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_084 : STELYQQLNDLEACVMQEERVGETPLMNADSILAVKKYFRRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_085 : STELYQQLNDLEACVMQEERVGETPLMNADSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_086 : YTELYQQLNDLEACVIQEVGVEETPLMNEDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_087 : YIELFQQMNDLEACVIQEVGVEETPLRNVDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_088 : STELYQQLNDLEACVMQEERVGETPLMNADSILAVKKYFRRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_089 : YTELNQQLNDLEACVIQEVGVEETPLMNEDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_090 : YIELDQQLNDLESCVMQEVGVEETPLINEDSILAVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
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Fig. 6N

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                 *        100         *        120         *        140         *        160
SEQ_091 : STELYQQLNDLEACVMQEERVGETPLMNADSILAVKKYFRRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_092 : YTELNQQLNDLEACVIQEVGVEETPLMNEDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_093 : STELYQQLNDLEACVMQEERVGETPLMNADSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_094 : STELYQQLNDLEACVIQEVWVGGTPLMNEDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_095 : STELYQQLNDLEACVIQEVGVEETPLMNVDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_096 : YTELYQQLNDLEACVMQEERVGETPLMNADSILAVKKYFRRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_097 : YTELYQQLNDLEACMMQEVGVEDTPLMNVDSILTVRKYFQRITLYLKEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_098 : STELNQQLNDLEACVMQEERVGETPLMNADSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_099 : YTELYQQLNDLEACVIQEVGVEEAPLMNEDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_100 : STELNQQLNDLEACVIQEVGVEETPLMNVDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_101 : YTELNQQLNDLEACVIQEVGVEETPLMNVDSILAVRKYFQRITLYLTEKKYSPCSWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_102 : YTELNQQLNDLEACVIQEVGVEETPLMNEDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_103 : STELYQQLNDLEACVMQEERVGETPLMNADSILAVKKYFRRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_104 : STELYQQLNDLEACVMQEERVGETPLMNADSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_105 : CTELNQQLNDLEACVIQEVGVEETPLMNVDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_106 : YTELNQQLNDLEACVIQEVGVEETPLMNEDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_107 : YIELFQQMNDLEACMMQEVGVEETPLRNVDSILAVKKYFQRITLYLMEKKYRPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_108 : YTELNQQLNDLEACVIQEVGVEETPLMNEDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_109 : YTELYQQLNDLEACVIQEVGMEETPLMNEDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_110 : YIELNQQLNDLEACVIQEVGVEETPLMNVDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_111 : SIEIYQQLNDLEACVIQEVGVEETPLMNVDSILAVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_112 : STELNQQLNDLEACVIQEVGMEETPLMNVDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_113 : STELYQQLNDLEACVMQEERVGETPLMNADSILAVKKYFRRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_114 : YIELDQQLNDLESCVMQEVGVEETPLMNVDSILTVRKYFQRITLYLTEKKYSPCSWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_115 : YTELYQQLNDLEACVMQKVGMEETPLMNADSILAVRKYFQRITLYLKEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_116 : STELYQQLNDLEACVIQEVGVEETPLMNVDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_117 : STELYQQLNDLEACVMQEERVGETPLMNADSILAVKKYFQRITLYLTEKKYSPCSWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_118 : YTELNQQLNDLEACVIQEVGVEETPLMNEDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_119 : YIELNQQLNDLEACVIQEVGVEEIALMNADSILAVKKYFRRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_120 : STELNQQLNDLEACVMQEERVGETPLMNADSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
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Fig. 6O

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                 *        100         *        120         *        140         *        160
SEQ_121 : YTELNQQLNDLEACVMQEERVGETPLMNADSILAVKKYFRRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_122 : STELYQQLNDLEACVMQEERVGETPLMNADSILAVKKYFRRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_123 : YTELYQQLNDLEACVIQEVGVEETPLMNADSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_124 : STELNQQLNDLEACVMQEERVGETPLMNADSILAVKKYFRRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_125 : STELNQQLNDLEACVIQEVGVEETPLMNVDSILAVKKYFRRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_126 : YTELYQQLNDLEACVMQKVGVEETPLMNADSTLAVRKYFQRITLYLKEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_127 : YIELNQQLNDLEACVIQEVGVEETPLMNEDFILAVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_128 : STEIYQQLNDLEACVIQEERVGETPLMNADSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_129 : CTELYQQLNDLEACVIQEVGVEETPLMNEDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_130 : YTELYQQLNDLEACVIQEVGVEETPLMNEDSILAVKKYFRRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_131 : YIELNQQLNDLEACVIQEVGVEETPLMNVDSILAVRKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_132 : YTELYQQLNDLEACVMQEERVGETPLMNADSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 165
SEQ_133 : YTELYQQLNDLEACVIQEVGVEETPLMNVDSILTVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_134 : YIELFQQLNDLEACVTQEVGVEETPLMNVDSILAVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_135 : YIELDQQLNDLEACVMQEERVGETPLMNEDSILAVRKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_136 : YTELNQQLNDLEACVIQEVGVEEIALMNEDSILAVKKYFRRITLYLTEKKYSPCSWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_137 : YTELNQQLNDLEACVIQEVGVEETPLMNADSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_138 : STELYQQLNDLEACVIQEVGVEETPLMNVDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_139 : STELYQQLNDLEACVIQEVGVEETPLMNADSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_140 : YTELNQQLNDLEACVIQEVGMEETPLMNVDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_141 : YTELYQQLNDLEACMMQEVGVEDTPLMNVDSILTVRKYFQRITLYLKEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_142 : YIELDQQLDDLEACVIQGVGVTETPLMNEDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_143 : YTELNQQLNDLEACVIQEVGVEETPLMNEDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_144 : YIELNQQLNDLEACVIQEVGVEETPLMNVDSILAVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_145 : STELYQQLNDLEACVMQEERVGETPLMNADSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_146 : YTELYQQLNDLGACVMQEERVGETPLMNEDSILAVRKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_147 : YIELDQQLNDLESCVMQEVGVEETPLMNVDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_148 : CTELNQQLNDLEACVIQEVGMEETPLMNEDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_149 : STELYQQLNDLEACVMQEERVGETPLMNADSILAVKKYFQRITLYLTEKKYSPCSWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_150 : YTELNQQLNDLEACVIQEVGVGETPLMNADSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
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Fig. 6P

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                  *        100         *        120         *        140         *        160
SEQ_151 : STELYQQLNDLEACVMQEERVGETPLMNADSILAVKKYFQRITLYLTEKKYSPCSWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_152 : YTELYQQLNDLEACVIQEVGVEETPLMNEDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_153 : YIELDQQLNDLEACMIQEVGVEETPLMNVDSILAVKKYFQRITLYLVGKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_154 : YTELNQQLNDLEACVIQEVGMEETPLMNADSILAVKKYFQRITLYLTEKKYSPCSWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_155 : YTELYQQLNDLEACVIQEVGVEETPLMNVDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_156 : YIELFQQLNDLEACVIQEVGVEETPLMNVDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_157 : STELYQQLNDLEACVIQEVGVTETPLRNVDSILAVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_158 : RTELYQQLNDLEACVTQEVGVEEIALMNEDSILAVRKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_159 : YIELDQQLNDLEACMIQEVGVEETPLMNVDSILAVKKYFQRITLYLVGKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_160 : YTELYQQLNDLEACMMQEVGVEDTPLMNVDSILTVRKYFQRITLYLKEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_161 : STELYQQLNDLEACVIQEVGVEETPLMNVDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_162 : STELNRQLNDLEACVTQEVGVEETPLMNADSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_163 : STELYQQLNDLEACVIQEVGVGETPLMNADSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_164 : YTELYQQLNDLEACVIQEVGVEETPLRNVDSILAVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_165 : YTELNQQLNDLEACVIQEVWVGGTPLMNEDSILAVRKYFQRITLYLMGKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_166 : YIELDQQLNDLEACMIQEVGVEETPLMNVDSILAVKKYFQRITLYLVGKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_167 : YIELDQQLNDLEACMIQEVGVEETPLMNEDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_168 : YTELYQQLNDLEACVIQEVGVEEIALMNEDSILAVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_169 : STELYQQLNDLEACVIQEVGVEETPLMNEDSILAVKKYFRRITLYLKEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_170 : STELYQQLNDLEACVIQEVGMEETPLMNEDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_171 : YIELYQQLNDLEACVIQEVGVTETPLMKEDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_172 : YTELNQQLNDLEACVIQEVGVEETPLMNVDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_173 : YIELYQQLNNLEACVIQEVGVEETPLMNEDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_174 : YTELYQQLNDLEACVIQEVGMEETPLMNVDSILAVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_175 : YTELYQQLNDLEACVIQEVGVEETPLMNVDSILTVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_176 : YIELFQQMNDLEACVTQEVGVEEIALMNVDSILAVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_177 : YIELFQQMNDLEACVIQEVGVEETPLMNVDSILAVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_178 : STELNQQLNDLEACVIQEVGVEETPLRNVDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_179 : YIELDQQLNDLEACMIQEVGVEETPLMNEDSILAVKKYFQRITLYLTEKKYSPCSWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_180 : YTELNQQLNDLEACVIQEVGVEETPLMNEDSILAVKKYFQRITLYLTGKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
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Fig. 6Q

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               *        100         *        120         *        140         *        160
SEQ_181 : YIELDQQLNDLEACMIQEVGVEETPLMNVDSILAVKKYFQRITLYLIEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_182 : YIELYQQLNDLEACVIQEVGVEETPLMNEDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_183 : STELYQQLNDLEACVMQEERVGETPLMNADSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_184 : STELYQQLNDLEACVMQEERVGETPLMNADSILAVKKYFRRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_185 : YTELYQQLNDLEACVIQEVGVEETPLMNVDSILTVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_186 : YTELFQQMNDLEACVIQEVGVEETPLMNEDSILAVKKYFRRITLYLKEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_187 : STELNQQLNDLEACVIQEVGVGETPLMNADSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_188 : YIELNQQLNDLEACVIQEVGVEETPLMNVDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_189 : YTELYQQLNDLEACVIQGVGVTETPLMNVDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_190 : STEIYQQLNDLEACVIQEVGVEETPLINVDPILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_191 : YTELYQQLNDLEACVIQEVGVEETPLMNEDSILAVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_192 : YIELNQQLNDLEACVIQEERVGETPLMNADSILAVKKYFRRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_193 : YIELFQQMNDLEACVIQEVGVEETPLMNEDSILAVRKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_194 : YTELYQQLNDLEACVIQEVGVEETPLMNVDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_195 : YTELNQQLNDLEACVIQEVGVEETPLMNVDSILAVRKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_196 : YIELFQQMNDLEACVIQGVGVTETPLMKEDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_197 : YIELNQQLNDLEACVIQEVGVEETPLMNVDSILAVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_198 : YIELFQQMNDLEACVMQEERVGETPLMNAASILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_199 : STELYQQLNDLEACVMQEERVGETPLMNADSILAVKKYFRRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_200 : YIELDQQLNDLEACMIQEVGVEETPLMNVDSILAVKKYFQRITLYLVGKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_201 : STELYQQLNDLEACVIQEVGVEETPLMNVDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_202 : STELYQQLNDLEACVMQEERVGETPLMNADSILAVKKYFQRITLYLTEKKYSPCSWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_203 : YTELYQQLNDLEACVIQEVGVEEIALMNEDSILAVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_204 : RTELYQQLNDLEACVMQEERVGETPLMNADSILAVKKYFQRITLYLTEKKYSPCSWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_205 : YIELDQQLNDLEACMIQEVGVEETPLMNVDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_206 : STELYQQLNDLEACVIQEVGVEETPLMNVDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_207 : STELYQQLNDLEACVIQEVGVEETPLMNEDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_208 : YIELDQQLNDLEACVIQEVGVEETPLRNVDSILAVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_209 : YTELYQQLNDLEACVIQGVG--ETPLMNEDSILAVRKYFQRITLYLVGKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 164
SEQ_210 : YIELFQQMNDLEACVIQGVGVTETPLMNEDSILAVRKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
```

Fig. 6R

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                  *        100         *        120         *        140         *        160
SEQ_211 : YTELYQQLNDLEACVIQEVGVEETPLMNEDSILAVRKYFQRITLYLKEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_212 : YTELNQQLNDLEACVIQEVGVEETPLMNEDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_213 : YIELDQQLNDLEACVIQEVGMEETPLMNEDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_214 : YIELFRQMNDLEACVIQEVGVEETPLRNVDSILAVRKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_215 : YIELDQQLNDLESCVMQEVGVEETPLINEDSILAVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_216 : YIELDQQLNDLESCVMQEVGVTGTPLMNEDSILAVKKYFQRITLYLMEKKYGPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_217 : YIELDQQLNDLESCVMQEERVGETPLMNADSILAVKKYFRRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_218 : STELNQQLNDLEACVMQEVGMEETPLMNEDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_219 : YIELDQQLNDLESCVMQEVGVIESPLMNEDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_220 : YIELDQQLNDLESCVMQEVGVIESPLMNEDSILAVKKYFRRIALYLTEKKYSPCAWEVVRAEIMRSFSFSANLQKRLRRKE : 166
SEQ_221 : YIELDQQLNDLESCVMQEVGVIESPLMNEDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_222 : CTELYQQLNDLEACVMQEERVGETPLMNADSILAVKKYFRRITLYLTEKKYSPCAWEVIRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_223 : STELYQQLNDLEACVMQEERVGETPLMNADSILAVKKYFQRITLYLTEKKYSPCSWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_224 : YIELDQQLNDLESCVMQEVGVIESPLMNEDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_225 : YIELFRQMNDLEACVIQEVGVEETPLRNVDSILAVRKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_226 : YIELFQQLNDLEACVIQEVGVEETPLRNVDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_227 : CTELYQQLNDLEACVIQEVGVEETPLMNEDSILAVKKYFRRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_228 : STELYQQLNDLEACVVQEVGVEETPLMNVDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_229 : YIELDQQLNDLESCVMQEVGVEETPLINEDSILAVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_230 : YIELDQQLNDLEACMIQEVGVEETPLMNVDSILAVKKYFQRITLYLVGKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_231 : YIELDQQLNDLESCVMQEVGVIESPLMNEDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_232 : YIELDQQLNDLESCVMQEVGVTGTPLMNEDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_233 : STELYQQLNDLEACVMQEVWVGGTPLMNEDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_234 : YIELYQQLNDLEACVIQEVGVEETPLMNVDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_235 : YIELDQQLNDLEACVILGVGVTETPLMKEDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_236 : YIELDQQLNDLESCVMQEVGVEETPLMNADSILAVKKYFRRITLYLTEMKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_237 : STELNQQLNDLEACVIQEVGVEETPLMNEDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_238 : YIELDQQLNDLESCVMQEVGVIESPLMNEDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_239 : YIELDQQLNDLESCVMQEVGVTGTPLRNVDSILAVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_240 : YIELDQQLNDLESCVMQEVGVIESPLMNEDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
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Fig. 6S

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                   *        100         *         120         *         140         *         160
SEQ_241 : YIELDQQLNDLESCVMQEVGVTGTPLMNEDSILAVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_242 : YTELYQQLNDLEACVMQGERVGETPLRNVDSILTVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_243 : YIELDQQLNDLESCVMQEVGVTGTPLMNEDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_244 : STELYQQLNDLEACVMQEERVGETPLMNADSILAVKKYFQRITLYLTEKKYSPCSWEVVRAEIMRSFSFSTTLQKRLRRKE : 166
SEQ_245 : YIELDQQLNDLESCVMQEVGVEETPLINEDSILAVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_246 : YIELDQQLNDLESCVMQEVGVTGTPLMNEDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_247 : STELYQQLNDLEACVIQGVGVTETPLMNVDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_248 : YIELFQQMNDLEACVIQEVGVEETPLRNVDSILAVRKYFQRITLYLTKKKYSPCSWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_249 : STELNQQLNDLEACVIQEVGVEETPLMNVDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_250 : YIELDQQLNDLESCVMQEVGVEETPLMNEDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_251 : YIELNQQLNDLEACVIQEVGVEETALMNVDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLEKRLRRKE : 166
SEQ_252 : YTELYQQLNDLGACVMQEERVGETPLMNEDSILAVRKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_253 : YIELFRQMNDLEACVIQEVGVEETPLRNVDSILAVRKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_254 : STELNQQLNDLEACVIQEVGVEETPLMNEDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_255 : STELYQQLNDLEACVIQEVGVEETPLMNEDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_256 : YIELDQQLNDLEACVILGVGVTETPLMKEDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_257 : STELYQQLNDLEACVMQKVGVEETPLRNVDSILAVKKYFQRITLYLTEKKYSSCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_258 : YTELDQQLNDLESCVIQEVGVEEIALMNEDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_259 : STELNQQLNDLEACVIQEVGVEETPLMNVDSILTVRKYFQRITLYLTEKKYSPCSWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_260 : STELYQQLNDLEACVVQEVGVEETPLMNVDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_261 : YIELNQQLNDLEACVIQEVGVEETPLMNVDSILAVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_262 : YIELDQQLNDLESCVMQEVGVTGTPLMNEDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_263 : YIELDQQLNDLESCVMQEVGVIESPLMNEDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 165
SEQ_264 : YTELDQQLNDLESCVMQEVGVTGAPLMNEDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_265 : YIELNQQLNDLEACVIQEVGVEETPLRNVDSILAVRKYFQRITLYLTEKKYSPCSWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_266 : YIELDQQLNDLESCVMQEVGVEETPLINEDSILAVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_267 : YTELYQQLNDLEACVIQEVGVEETPLMNEDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_268 : YTELYQQLNDLEACVIQEVGVEETPLMNEDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_269 : YTELYQQLNDLEACVIQEVGVGETPLMNVDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_270 : YTELYQQLNDLEACVIQEVGVGETPLMNADSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
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Fig. 6T

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                  *         100         *         120         *         140         *         160
SEQ_271 : YTELNQQLNDLEACVIQEVGVEETPLMNVDSILAVKKYFRRITLYLMEKKYSPCAWEVVRAEIMRSLSFSTNLQKRLRRKE : 166
SEQ_272 : YIELNQQLNDLEACVIQEVGVEETPLMNVDSILAVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_273 : STELYQQLNDLEACVIQEVGVGETPLMNADSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_274 : YIELDQQLNDLESCVMQEVGVEETPLINVDPILAVRKYFQRITLYLTKKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_275 : YTELYQQLNDLEACVTQEVGMEETPLRNVDSILAVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_276 : STEIYQQLNDLEACVIQEVGVEETPLMNVDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_277 : YIELDQQLNDLESCVMQEVGVEETPLINEDSILAVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_278 : YTELNQQLNDLEACVIQEVGVEETPLMNVDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_279 : STELYQQLNDLEACVIQEVGVEETPLMNVDSILAVRKYFQRITLYLTEKKYSPCAWEVVRTEIMRSFSFSTNLQKRLRRKE : 166
SEQ_280 : YIELNQQLNDLEACVIQEVGVEETPLMNVDSILAVRKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_281 : YIELFQQLNDLEACVMQEERVGETPLMNADSILAVKKYFRRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_282 : STELYQQLNDLEACVIQEVGVGETPLMNADSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_283 : STELYQQLNDLEACVIQEVGMEETPLMNADSILAVKKYFRRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_284 : STELYQQLNDLEACVMQEERVGETPLMNADSILAVKKYFRRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_285 : YIELYQQLNDLEACVIQEVGVGETPLMNADSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_286 : YTELYQQLNDLEACVMQEVGVEDTPLMNVDSILAVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_287 : YTELYQQLNALEACVIQEVGVEETPLMNVDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_288 : STELYQQLNDLEACVMQEERVGETPLMNADSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_289 : STELYQQLNDLEACVMQEERVGETPLMNADSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_290 : STELYQQLNDLEACVMQEERVGETPLMNADSILAVKKYFRRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_291 : YIELFQQLNDLEACVIQEVGVEETPLMNVDSILTVRKYFQRITLYLTEKKYSPCSWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_292 : YIELNQQLNDLEACVIQEVGVEETPLMNVDSILAVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_293 : YIELDQQLNDLEACVMQEVWVGGTPLMNEDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_294 : YIELDQQLNDLESCVMQEVGVIESPLMNEDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_295 : STELYQQLNDLEACVMQEERVGETPLMNADSILAVKKYFRRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_296 : STELYQQLNDLEACVMQEERVGETPLMNADSILAVKKYFRRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_297 : YIELDQQLNDLESCVMQEVGVTGTPLMNEDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_298 : YTELNQQLNDLEACVIQEVGVEETPLMNEDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_299 : YIELNQQLNDLEACVIQEVGVEETPLMNVDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_300 : STELYQQLNDLEACVTQEVGVEEIALMNEDSILAVRKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
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Fig. 6U

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                *        100         *        120         *        140         *        160
SEQ_301 : YIELFQQMNDLEACVIQEVGVEETPLRNVDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_302 : STELYRQLNDLEACVIQEVGVEETPLMNADSILPVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_303 : YIELDQQLNDLEACVILGVGVTETPLMKEDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_304 : YIELDQQLNDLESCVMQEVGVTGTPLMNEDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKGLRRKE : 166
SEQ_305 : YIELDQQLNDLESCVMQEVGVIESPLMNEDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_306 : YIELDQQLNDLEACMIQEVGVEETPLMNVDSILAVKKYFQRITLYLVGKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_307 : STELYQQLNDLEACVIQEVGVEETPLMNVDSILAVRKYFQRITLYLTGKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_308 : YIELDQQLNDLEACMIQEVGVEETPLMNVDSILAVKKYFQRITLYLVGKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_309 : STELYQQLNDLEACVMQEERVGETPLMNADSILAVKKYFQRITLYLTEKKYSPCSWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_310 : YIELDQQLNDLESCVMQEVGVTGTPLMNEDSILAVKKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_311 : STELYQQLNDLEACVMQEVWVGGTPLMNEDSILAVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_312 : YIELDQQLNDLESCVMQEVGVTGTPLMNEDSILAVKKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_313 : YVELDQQLNDLEACVIQEVGVEEIALMNEDFILAVRKYFQRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_314 : STELYQQLNDLEACVMQEERVGETPLMNADSILAVKKYFRRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_315 : YIELDQQLNDLEACMIQEVGVEETPLMNEDSILAVKKYFQRITLYLTKKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_316 : STELNQQLNDLEACVIQEVGVEETPLMNVDSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_317 : STELYQQLNDLEACVIQEVGVGETPLMNADSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_318 : STELYQQLNDLEACVIQEVGVGETPLMNADSILAVKKYFRRITLYLTEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
SEQ_319 : YIELNQQLNDLEACVIQEVGVEETPLMNVDSILAVRKYFQRITLYLMEKKYSPCAWEVVRAEIMRSFSFSTNLQKRLRRKE : 166
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Fig. 6V

SEQUENCE LISTING

<110> Maxygen, Inc.

<120> EVOLVED INTERFERON-ALPHA POLYPEPTIDES

<130> 0284.210WO

<150> US 60/682,769
<151> 2005-05-18

<160> 335

<170> FastSEQ for Windows Version 4.0

<210> 1
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 1
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20 25 30
Arg His Asp Phe Gly Leu Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Arg Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Ala Asp Ser Ile Leu Pro Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 2
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 2
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15

Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Leu Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Leu Asp Glu Thr
65 70 75 80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Met Gln Glu Val Trp Val Gly Gly Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Ser Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 3
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 3
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Leu Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Arg Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 4
<211> 166
<212> PRT
<213> Artificial Sequence

<220>

<223> Synthetic IFN-alpha Polypeptide

<400> 4
```
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
 1               5                  10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Leu Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Leu Asp Glu Thr
65                  70                  75                  80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Met Gln Glu Val Trp Val Gly Gly Thr Pro Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 5
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 5
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Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
 1               5                  10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Leu Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Trp Asp Glu Asp
65                  70                  75                  80
Leu Leu Asp Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Met Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Val Gly Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
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<210> 6

<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 6
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Leu Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Leu Asp Glu Thr
65 70 75 80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Met Gln Glu Val Trp Val Gly Gly Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 7
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 7
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser His Phe Ser Cys Leu Lys Asp
20 25 30
Arg Tyr Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly His Gln Phe
35 40 45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Glu Phe Tyr Val Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Ile Ala Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160

Arg Leu Arg Arg Lys Glu
165

<210> 8
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 8
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Leu Ile Gln Gln Ala
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Leu Asp Glu Thr
65 70 75 80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Met Gln Glu Val Trp Val Gly Gly Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 9
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 9
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg Tyr Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ser Cys Val Met Gln Glu Val Gly Val Ile Glu Ser Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr

```
        115                     120                     125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 10
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 10

```
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
 1               5                  10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg Tyr Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly His Gln Phe
        35                  40                  45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Trp Asp Glu Asp
65                  70                  75                  80
Leu Leu Asp Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Met Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 11
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 11

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Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
 1               5                  10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Leu Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Leu Asp Glu Thr
65                  70                  75                  80
```

Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Met Gln Glu Val Trp Val Gly Gly Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 12
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 12
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Thr Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Pro Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Arg
65 70 75 80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ser Cys Val Met Gln Glu Val Gly Val Thr Gly Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 13
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 13
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe

35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Leu Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ser Cys Val Met Gln Glu Val Gly Val Ile Glu Ser Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 14
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 14
Cys Asp Leu Pro Gln Thr His Ser Leu Asp Asn Arg Arg Thr Leu Met
1 5 10 15
Leu Leu Ala Gln Met Ser Arg Ile Ser Pro Ser Ser Cys Leu Met Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Ala Phe His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Trp Asp Glu Asp
65 70 75 80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Ile Glu Ser Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 15
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 15

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Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Glu Phe Arg Phe Pro Glu Glu Glu Phe Asp Gly His Gln Phe
        35                  40                  45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Asp Thr Trp Asp Ala Thr
65                  70                  75                  80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Leu Gly Val Gly Val Thr Glu Thr Pro Leu Met
            100                 105                 110
Lys Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 16
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 16

```
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1               5                   10                  15
Leu Leu Ala Arg Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly His Gln Phe
        35                  40                  45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Met Gln Glu Val Trp Val Gly Gly Thr Pro Leu Met
            100                 105                 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 17
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 17
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg Tyr Asp Phe Glu Phe Pro Gln Glu Glu Phe Asp Gly His Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Met Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ser Cys Val Met Gln Glu Val Gly Val Ile Glu Ser Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 18
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 18
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Leu Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Arg Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

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<210> 19
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 19
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Pro Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ser Cys Val Met Gln Glu Val Gly Val Ile Glu Ser Pro Leu Met
            100                 105                 110
Lys Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165


<210> 20
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 20
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Glu Phe Arg Phe Pro Glu Glu Glu Phe Asp Ser Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Asp Thr Trp Asp Ala Thr
65                  70                  75                  80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Leu Gly Val Gly Val Thr Glu Thr Pro Leu Met
            100                 105                 110
Lys Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
```

Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 21
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 21
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Leu Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Leu Asp Glu Thr
65 70 75 80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Met Gln Glu Val Trp Val Gly Gly Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 22
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 22
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Pro Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Ala Thr
65 70 75 80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Leu Gly Val Gly Val Thr Glu Thr Pro Leu Met

```
            100                 105                 110
Lys Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 23
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 23

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Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Gly Thr Lys Asn Ser Ser Ala Ala Trp Asp Glu Asp
65                  70                  75                  80
Leu Leu Asp Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Met Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 24
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 24

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Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
```

```
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Asp Glu Phe Tyr Val Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Ala Asp Ser Ile Leu Pro Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165


<210> 25
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 25
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
 1              5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Leu Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Asp Glu Phe Tyr Val Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Ile Ala Leu Met
            100                 105                 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165


<210> 26
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 26
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
 1              5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
```

20 25 30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Val Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Met Gln Glu Val Trp Val Gly Gly Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 27
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 27
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly His Gln Phe
35 40 45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Asp Thr Trp Asp Ala Thr
65 70 75 80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Leu Gly Val Gly Val Thr Glu Thr Pro Leu Met
100 105 110
Lys Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 28
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 28
```
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Pro Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 29
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 29
```
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Ser Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Asp Thr Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Met Gln Glu Val Trp Val Gly Gly Thr Pro Leu Met
            100                 105                 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 30
<211> 166

<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 30
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Glu Phe Arg Phe Pro Glu Glu Glu Phe Asp Gly His Gln Phe
35 40 45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Met Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 31
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 31
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Phe Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Ser Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Trp Asp Glu Asp
65 70 75 80
Leu Leu Asp Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asp Asp Leu
85 90 95
Glu Ala Cys Met Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Val Gly Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu

165

<210> 32
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 32
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Pro Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Glu Phe Tyr Val Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 33
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 33
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Arg Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Met Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ser Cys Val Met Gln Glu Val Gly Val Ile Glu Ser Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125

```
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165


<210> 34
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 34
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser His Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Val Ala Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Asp His Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Thr Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165


<210> 35
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 35
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Pro Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
```

```
                85                      90                      95
Glu Ser Cys Val Met Gln Glu Val Gly Val Ile Glu Ser Pro Leu Met
            100                     105                     110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                     120                     125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                     135                     140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                     150                     155                     160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 36
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 36

```
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Phe Ile
 1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Trp Asp Glu Asp
65                  70                  75                  80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 37
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 37

```
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
 1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser His Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg Tyr Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly His Gln Phe
        35                  40                  45
```

Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Glu Phe Tyr Val Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Ile Ala Leu Ile
100 105 110
Asn Glu Asp Phe Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 38
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 38
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Pro Ala Ile Ser Val Leu His Glu Leu Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ser Cys Val Met Gln Glu Val Gly Val Ile Glu Ser Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 39
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 39
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile

1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly His Gln Phe
35 40 45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Arg
65 70 75 80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ser Cys Val Met Gln Glu Val Gly Val Ile Glu Ser Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 40
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 40
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly His Gln Phe
35 40 45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Leu Gly Val Gly Val Thr Glu Thr Pro Leu Met
100 105 110
Lys Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 41
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 41
```
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Leu Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ser Cys Val Met Gln Glu Val Gly Val Ile Glu Ser Pro Leu Met
            100                 105                 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 42
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 42
```
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Pro Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Met Gln Glu Val Trp Val Gly Gly Thr Pro Leu Met
            100                 105                 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 43
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 43
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Leu Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Leu Asp Glu Thr
65 70 75 80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 44
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 44
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Arg Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Ala Asp Ser Ile Leu Pro Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys

145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 45
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 45
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Pro Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ser Cys Val Met Gln Glu Val Gly Val Ile Glu Ser Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 46
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 46
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly His Gln Phe
35 40 45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Arg
65 70 75 80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Met Glu Glu Thr Pro Leu Met
100 105 110

Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 47
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 47
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Phe Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Trp Asp Glu Asp
65 70 75 80
Leu Leu Asp Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Met Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 48
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 48
Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Met Met
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Leu Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Leu Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Leu Asp Glu Thr

```
65                  70                  75                  80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Met Gln Glu Val Trp Val Gly Gly Thr Pro Leu Met
            100                 105                 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 49
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 49

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Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
 1               5                  10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Leu Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Gly Thr Lys Asn Ser Ser Ala Ala Leu Asp Glu Thr
65                  70                  75                  80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Met Gln Glu Val Trp Val Gly Gly Thr Pro Leu Met
            100                 105                 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 50
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 50

```
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
 1               5                  10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
```

```
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Pro Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ser Cys Val Met Gln Glu Val Gly Val Ile Glu Ser Pro Leu Met
            100                 105                 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165


<210> 51
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 51
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
 1               5                  10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Pro Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ser Cys Val Met Gln Glu Val Gly Val Ile Glu Ser Pro Leu Met
            100                 105                 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Val Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165


<210> 52
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide
```

<400> 52
```
Cys Asp Leu Pro Gln Thr His Ser Leu Asp Asn Arg Arg Thr Leu Met
1               5                   10                  15
Leu Leu Ala Gln Met Ser Arg Ile Ser Pro Ser Ser Cys Leu Met Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Val Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Asp Thr Trp Asp Ala Thr
65                  70                  75                  80
Leu Leu Asp Lys Phe Tyr Ile Glu Leu Phe Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Thr Gln Glu Val Gly Val Glu Glu Ile Ala Leu Met
            100                 105                 110
Asn Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 53
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 53
```
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Leu Asp Glu Thr
65                  70                  75                  80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Asn Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Ala Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Ser Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 54
<211> 166
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 54
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Phe Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Arg Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Thr Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Met Glu Glu Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 55
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 55
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser His Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly His Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Glu Lys Phe Cys Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
100 105 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 56
<211> 165
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 56
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Thr Leu Met
1 5 10 15
Leu Leu Ala Gln Met Ser Arg Ile Ser Pro Ser Ser Cys Leu Met Asp
20 25 30
Arg Tyr Asp Phe Glu Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
35 40 45
Lys Val Gln Ala Ile Phe Leu Phe His Glu Met Ile Gln Gln Thr Phe
50 55 60
Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
65 70 75 80
Leu Asp Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu Glu
85 90 95
Ser Cys Val Met Gln Glu Val Gly Val Ile Glu Ser Pro Leu Met Tyr
100 105 110
Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
115 120 125
Tyr Leu Thr Glu Arg Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
130 135 140
Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys Arg
145 150 155 160
Leu Arg Arg Lys Glu
165

<210> 57
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 57
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Glu Phe Arg Phe Pro Glu Glu Glu Phe Asp Gly His Gln Phe
35 40 45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val

130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 58
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 58
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Gly Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Ile Pro Gln Glu Val Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
100 105 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 59
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 59
Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Met Met
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
85 90 95

```
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
            100                 105                 110
Asn Val Asp Ser Val Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 60
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 60

```
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Met Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys His Ser Ser Ala Thr Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ser Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 61
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 61

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Cys Asp Leu Pro Gln Thr His Ser Leu Arg Ser Arg Arg Thr Leu Met
1               5                   10                  15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Leu Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
```

```
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys His Ser Ser Ala Thr Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Asp Lys Phe Tyr Ile Glu Leu Asn Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Ile
            100                 105                 110
Asn Val Asp Pro Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165


<210> 62
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 62
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Met Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys His Ser Ser Ala Thr Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Asp Lys Phe Tyr Ile Glu Leu Asn Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Ile Ala Leu Met
            100                 105                 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165


<210> 63
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 63
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1               5                   10                  15
```

Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Glu Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Thr Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Gly Glu Thr Pro Leu Met
100 105 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Asn Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 64
<211> 165
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 64
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
35 40 45
Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Met Gln Gln Thr Phe
50 55 60
Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Trp Asp Glu Thr Leu
65 70 75 80
Leu Asp Lys Leu Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
85 90 95
Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Ile Ala Leu Met Asn
100 105 110
Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
115 120 125
Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
130 135 140
Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys Arg
145 150 155 160
Leu Arg Arg Lys Glu
165

<210> 65
<211> 166
<212> PRT
<213> Artificial Sequence

<220>

<223> Synthetic IFN-alpha Polypeptide

<400> 65
```
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1               5                   10                  15
Leu Leu Ala Gln Met Arg Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Glu Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Trp Asp Glu Asp
65                  70                  75                  80
Leu Leu Asp Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Met Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Val Gly Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 66
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 66
```
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Thr Trp Glu Gln Ser
65                  70                  75                  80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
            100                 105                 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 67

<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 67
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Glu Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Arg
100 105 110
Asn Val Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 68
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 68
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Glu Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Ala Phe His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Ile Glu Leu Phe Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
100 105 110
Asn Val Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160

Arg Leu Arg Arg Lys Glu
165

<210> 69
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 69
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Ile Pro Gln Glu Val Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Val Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 70
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 70
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Gly Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Ile Pro Gln Glu Val Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Lys Leu Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Ile Ala Leu Met
100 105 110
Asn Glu Gly Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr

```
        115                     120                     125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

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<210> 71
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 71
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Glu Phe Arg Phe Pro Glu Glu Glu Phe Asp Gly His Gln Phe
        35                  40                  45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Trp Asp Glu Asp
65                  70                  75                  80
Leu Leu Asp Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Met Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Val Gly Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

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<210> 72
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 72
Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Met Met
1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly His Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Asp Glu Thr
65                  70                  75                  80
```

```
Leu Leu Asp Lys Leu Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Ile Ala Leu Met
            100                 105                 110
Asn Glu Gly Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165


<210> 73
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 73
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
 1               5                  10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Arg Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ser Cys Val Met Gln Glu Val Gly Val Ile Glu Ser Pro Leu Met
            100                 105                 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165


<210> 74
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 74
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
 1               5                  10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Arg Phe Pro Gln Glu Glu Phe Asp Ser Asn Gln Phe
```

```
        35                   40                   45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Asp Thr Trp Asp Ala Thr
65                  70                  75                  80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Leu Gly Val Gly Val Thr Glu Thr Pro Leu Met
            100                 105                 110
Lys Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 75
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 75

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Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Met Met
1               5                   10                  15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly His Gln Phe
        35                  40                  45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65                  70                  75                  80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
            100                 105                 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 76
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 76

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Cys Asp Leu Pro Gln Thr His Ser Leu Ser Asn Arg Arg Ala Phe Ile
1               5                   10                  15
Leu Leu Thr Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly His Gln Phe
        35                  40                  45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65                  70                  75                  80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Asn Arg Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Thr Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 77
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 77

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Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly His Gln Phe
        35                  40                  45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Arg
65                  70                  75                  80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ser Cys Val Met Gln Glu Val Gly Val Thr Gly Thr Pro Leu Met
            100                 105                 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys His Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 78
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 78
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Glu Gly Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Met Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Asp Thr Trp Asp Glu Thr
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 79
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 79
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Phe Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Met Met Gln Lys Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 80
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 80
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Val Asp Ser Ile Leu Thr Val Arg Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ser Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 81
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 81
Cys Asp Leu Pro Gln Thr His Ser Leu Ser Asn Arg Arg Thr Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Glu Phe Pro Gln Glu Glu Phe Asp Asp Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Met Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys His Ser Ser Ala Thr Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Ile Glu Leu Asn Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140

```
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165


<210> 82
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 82
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
 1               5                  10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Arg Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Arg Lys Ala Glu Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165


<210> 83
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 83
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met
 1               5                  10                  15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Glu Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Val Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
```

100 105 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 84
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 84
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Thr Met Met
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Glu Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
100 105 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 85
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 85
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Gly Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Val Gln Gln Thr
50 55 60

Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
100 105 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 86
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 86
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Leu Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 87
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 87
Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Met Met
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp

```
                20                      25                      30
Arg His Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                      40                      45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Met Gln Gln Thr
    50                      55                      60
Phe Asn Leu Phe Ser Thr Lys His Ser Ser Ala Ala Trp Asp Glu Thr
65                  70                      75                  80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Phe Gln Gln Met Asn Asp Leu
                85                      90                      95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Arg
                100                     105                     110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                     120                     125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                     135                     140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                     155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 88
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 88

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Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1               5                   10                      15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                      30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                      45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                      60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65                  70                      75                  80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                      90                      95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
            100                     105                     110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                     120                     125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                     135                     140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                     155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 89
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 89
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly His Gln Val
35 40 45
Gln Lys Val Gln Ala Ile Phe Leu Phe His Glu Val Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys His Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 90
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 90
Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Met Met
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Thr Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ser Cys Val Met Gln Glu Val Gly Val Glu Glu Thr Pro Leu Ile
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 91
<211> 166

<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 91
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Asp Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
100 105 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 92
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 92
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Gly Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu

165

<210> 93
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 93
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Val Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
100 105 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 94
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 94
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly His Gln Phe
35 40 45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Met Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Trp Val Gly Gly Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125

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Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
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<210> 95
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 95

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Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Met Met
 1               5                  10                  15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Arg Phe Pro Gln Glu Glu Phe Asp Gly His Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Leu Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65                  70                  75                  80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
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<210> 96
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 96

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Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
 1               5                  10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Val Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
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                85   90   95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
            100   105   110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115   120   125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130   135   140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145   150   155   160
Arg Leu Arg Arg Lys Glu
                165

<210> 97
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 97
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
 1   5   10   15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20   25   30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly His Gln Phe
        35   40   45
Gln Lys Ala Glu Ala Ile Ser Val Leu His Glu Met Met Gln Gln Thr
    50   55   60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Thr Trp Asp Ala Thr
65   70   75   80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85   90   95
Glu Ala Cys Met Met Gln Glu Val Gly Val Glu Asp Thr Pro Leu Met
            100   105   110
Asn Val Asp Ser Ile Leu Thr Val Arg Lys Tyr Phe Gln Arg Ile Thr
        115   120   125
Leu Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130   135   140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145   150   155   160
Arg Leu Arg Arg Lys Glu
                165

<210> 98
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 98
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Ala Leu Ile
 1   5   10   15
Leu Leu Gly Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20   25   30
Arg His Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35   40   45

Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
100 105 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 99
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 99
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Asp Thr Trp Asp Ala Asp
65 70 75 80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Ala Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 100
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 100
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Thr Met Met

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1               5                   10                  15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Leu Pro Gln Glu Glu Phe Asp Gly His Gln Phe
        35                  40                  45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Leu Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Thr Trp Glu Gln Ser
65                  70                  75                  80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
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<210> 101
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 101
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1               5                   10                  15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Glu Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Pro Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Thr Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ser Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165


<210> 102
<211> 166
<212> PRT
<213> Artificial Sequence
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<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 102
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Glu Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Glu Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 103
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 103
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Gly Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Ile Pro Gln Glu Val Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
100 105 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 104
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 104
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Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Met Met
 1               5                  10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65                  70                  75                  80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
            100                 105                 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
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<210> 105
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 105
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Cys Asp Leu Pro Gln Thr His Ser Leu Ser Asn Arg Arg Thr Leu Ile
 1               5                  10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Glu Phe Pro Gln Glu Glu Phe Asp Asp Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Glu Gln Ser
65                  70                  75                  80
Leu Leu Asp Lys Phe Cys Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
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145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 106
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 106
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Met
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly His Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 107
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 107
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Phe Gln Gln Met Asn Asp Leu
85 90 95
Glu Ala Cys Met Met Gln Glu Val Gly Val Glu Glu Thr Pro Leu Arg
100 105 110

Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115   120   125
Leu Tyr Leu Met Glu Lys Lys Tyr Arg Pro Cys Ala Trp Glu Val Val
    130   135   140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145   150   155   160
Arg Leu Arg Arg Lys Glu
                165

<210> 108
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 108
Cys Asp Leu Pro Gln Thr His Ser Leu Ser Asn Arg Arg Thr Leu Ile
1   5   10   15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20   25   30
Arg His Asp Phe Glu Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35   40   45
Gln Lys Ala Glu Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
    50   55   60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65   70   75   80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
                85   90   95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100   105   110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115   120   125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130   135   140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145   150   155   160
Arg Leu Arg Arg Lys Glu
                165

<210> 109
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 109
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1   5   10   15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20   25   30
Arg His Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35   40   45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Val Gln Gln Thr
    50   55   60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser

65 70 75 80
Leu Leu Glu Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Met Glu Glu Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 110
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 110
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Glu Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Pro Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Asn Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 111
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 111
Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Met Met
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30

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Arg His Asp Phe Glu Phe Pro Gln Glu Glu Phe Asp Gly His Gln Phe
        35                  40                  45
Gln Lys Thr Gln Ala Val Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Thr Trp Glu Gln Ser
65                  70                  75                  80
Leu Leu Glu Lys Phe Ser Ile Glu Ile Tyr Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
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<210> 112
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 112

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Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
 1              5                   10                  15
Leu Leu Gly Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Arg Ile Pro Gln Glu Val Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Glu Gln Ser
65                  70                  75                  80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Met Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
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<210> 113
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 113
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
100 105 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 114
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 114
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg Gln Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Thr Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ser Cys Val Met Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Val Asp Ser Ile Leu Thr Val Arg Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ser Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 115
<211> 166
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 115

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Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Leu Ile
1               5                   10                  15
Leu Leu Ala Gln Met Arg Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Leu Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Asp Thr Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Met Gln Lys Val Gly Met Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Ala Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
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<210> 116
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 116

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Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Val Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65                  70                  75                  80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
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<210> 117
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 117
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
100 105 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ser Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 118
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 118
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val

130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 119
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 119
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Thr Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Gln Gly Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Met Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys His Ser Ser Ala Thr Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Ile Glu Leu Asn Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Ile Ala Leu Met
100 105 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 120
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 120
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Gly Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
85 90 95

Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
100 105 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 121
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 121
Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Leu Met
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly His Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Val Met Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
100 105 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 122
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 122
Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Met Met
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Phe Pro Gln Glu Glu Phe Asp Gly His Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr

50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
100 105 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 123
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 123
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Thr Met Met
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Asp Thr Trp Asp Ala Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 124
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 124
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15

Leu Leu Gly Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Ile Pro Gln Glu Val Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
100 105 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 125
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 125
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Gly Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Ile Pro Arg Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Glu Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Thr Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 126
<211> 166
<212> PRT
<213> Artificial Sequence

<220>

<223> Synthetic IFN-alpha Polypeptide

<400> 126
Cys Asp Leu Pro Gln Thr His Ser Leu Asn Asn Arg Arg Thr Leu Met
1   5   10   15
Leu Met Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20   25   30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35   40   45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Met Gln Gln Thr
    50   55   60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Thr Trp Asp Glu Thr
65   70   75   80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85   90   95
Glu Ala Cys Val Met Gln Lys Val Gly Val Glu Glu Thr Pro Leu Met
            100   105   110
Asn Ala Asp Ser Thr Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
        115   120   125
Leu Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130   135   140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145   150   155   160
Arg Leu Arg Arg Lys Glu
                165

<210> 127
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 127
Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Met Met
1   5   10   15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20   25   30
Arg His Asp Phe Arg Ile Pro Gln Glu Val Phe Asp Gly Asn Gln Phe
        35   40   45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50   55   60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65   70   75   80
Leu Leu Asp Lys Phe Tyr Ile Glu Leu Asn Gln Gln Leu Asn Asp Leu
                85   90   95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100   105   110
Asn Glu Asp Phe Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
        115   120   125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130   135   140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145   150   155   160
Arg Leu Arg Arg Lys Glu
                165

<210> 128

<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 128
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Gly Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Ile Pro Gln Glu Val Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Ile Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
100 105 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 129
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 129
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Gly Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Asp Lys Phe Cys Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160

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Arg Leu Arg Arg Lys Glu
                165


<210> 130
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 130
Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Met Met
1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Met Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165


<210> 131
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 131
Cys Asp Leu Pro Gln Thr His Ser Leu Ser Asn Arg Arg Thr Leu Ile
1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Glu Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Met Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys His Ser Ser Ala Thr Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Asp Lys Phe Tyr Ile Glu Leu Asn Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
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Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
115 120 125
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
130 135 140
Arg Leu Arg Arg Lys Glu
145 150 155 160
165

<210> 132
<211> 165
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 132
Cys Asp Leu Pro Gln Thr His Ser Leu Ser Asn Arg Arg Thr Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Glu Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
35 40 45
Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Thr Phe
50 55 60
Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser Leu
65 70 75 80
Leu Glu Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
85 90 95
Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met Asn
100 105 110
Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr Leu
115 120 125
Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
130 135 140
Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys Arg
145 150 155 160
Leu Arg Arg Lys Glu
165

<210> 133
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 133
Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Met Met
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Leu Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80

Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Val Asp Ser Ile Leu Thr Val Arg Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 134
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 134
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Phe Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Thr Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Val Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 135
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 135
Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Met Met
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe

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        35                  40                  45
Gln Lys Ala Glu Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Asp Thr Trp Asp Ala Thr
65                  70                  75                  80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
            100                 105                 110
Asn Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
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<210> 136
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 136
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Thr Met Met
1               5                   10                  15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Ile Ala Leu Met
            100                 105                 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ser Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
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<210> 137
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 137
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Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Thr Met Met
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 138
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 138
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Gly Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Ile Pro Glu Glu Glu Phe Asp Gly His Gln Phe
35 40 45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Asp Thr Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 139
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 139
Cys Asp Leu Pro Gln Thr His Ser Leu Ser Asn Arg Arg Thr Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Glu Phe Pro Gln Glu Glu Phe Asp Asp Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 140
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 140
Cys Asp Leu Pro Gln Thr His Ser Leu Ser Asn Arg Arg Thr Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Glu Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Thr Trp Asp Ala Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Met Glu Glu Thr Pro Leu Met
100 105 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 141
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 141
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Met Met
1   5   10   15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20   25   30
Arg His Asp Phe Glu Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35   40   45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50   55   60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Thr Trp Asp Ala Thr
65   70   75   80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85   90   95
Glu Ala Cys Met Met Gln Glu Val Gly Val Glu Asp Thr Pro Leu Met
            100   105   110
Asn Val Asp Ser Ile Leu Thr Val Arg Lys Tyr Phe Gln Arg Ile Thr
        115   120   125
Leu Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130   135   140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145   150   155   160
Arg Leu Arg Arg Lys Glu
                165

<210> 142
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 142
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1   5   10   15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20   25   30
Arg Tyr Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35   40   45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50   55   60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65   70   75   80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asp Asp Leu
                85   90   95
Glu Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met
            100   105   110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115   120   125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130   135   140

Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 143
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 143
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Ile Pro Gln Glu Val Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 144
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 144
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Thr Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Ile Glu Leu Asn Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met

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                100                       105                       110
Asn Val Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
            115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                     160
Arg Leu Arg Arg Lys Glu
                165
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<210> 145
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 145

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Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1               5                   10                  15
Leu Leu Gly Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65                  70                  75                  80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
            100                 105                 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
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<210> 146
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 146

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Cys Asp Leu Pro Gln Thr His Ser Leu Ser Asn Arg Arg Thr Leu Ile
1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Glu Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
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Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Thr Trp Asp Ala Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Gly Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 147
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 147
Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Met Met
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Glu Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Thr Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ser Cys Val Met Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 148
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 148
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp

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                20                      25                      30
Arg His Asp Phe Gly Leu Pro Gln Glu Glu Phe Asp Gly His Gln Phe
            35                      40                      45
Gln Lys Ala Glu Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
        50                      55                      60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65                      70                      75                      80
Leu Leu Asp Lys Phe Cys Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
                85                      90                      95
Glu Ala Cys Val Ile Gln Glu Val Gly Met Glu Glu Thr Pro Leu Met
            100                     105                     110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                     120                     125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                     135                     140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                     150                     155                     160
Arg Leu Arg Arg Lys Glu
                165
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<210> 149
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 149

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Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Val Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65                  70                  75                  80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
            100                 105                 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ser Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
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<210> 150
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 150
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Thr Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Glu Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Gly Glu Thr Pro Leu Met
100 105 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 151
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 151
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Ile Pro Gln Glu Val Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Glu Ala Ile Ser Val Leu His Glu Met Val Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
100 105 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ser Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 152
<211> 166

<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 152
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Glu Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Thr Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 153
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 153
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Thr Met Met
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Trp Asp Glu Asp
65 70 75 80
Leu Leu Asp Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Met Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Val Gly Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu

165

<210> 154
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 154
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Leu Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Asp Thr Trp Asp Ala Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Met Glu Glu Thr Pro Leu Met
100 105 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ser Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 155
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 155
Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Met Met
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Asp Thr Trp Asp Ala Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125

Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 156
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 156
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Met
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg Gln Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Met Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Phe Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 157
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 157
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly His Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Leu Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu

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                            85                       90                       95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Thr Glu Thr Pro Leu Arg
                100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
            115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
        130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
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<210> 158
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 158

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Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Gly Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Asp
65                  70                  75                  80
Leu Leu Asp Lys Phe Arg Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Thr Gln Glu Val Gly Val Glu Glu Ile Ala Leu Met
            100                 105                 110
Asn Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
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<210> 159
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 159

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Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Arg Ile Pro Arg Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
```

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Gln Lys Ala Glu Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Asp
65                  70                  75                  80
Leu Leu Asp Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Met Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Val Gly Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
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<210> 160
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 160

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Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Met Met
1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Glu Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Met Met Gln Glu Val Gly Val Glu Asp Thr Pro Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Thr Val Arg Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
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<210> 161
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 161

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Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
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 1               5                   10                  15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Glu Gln Ser
65                  70                  75                  80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
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<210> 162
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 162

```
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
 1               5                   10                  15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Arg Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Met Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65                  70                  75                  80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Asn Arg Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Thr Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
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<210> 163
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 163
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Glu Gly Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Gly Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Gly Glu Thr Pro Leu Met
100 105 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 164
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 164
Cys Asp Leu Pro Gln Thr His Ser Leu Asp Asn Arg Arg Thr Leu Met
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Ile Pro Gln Glu Val Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Arg
100 105 110
Asn Val Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 165
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 165
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Leu Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Trp Val Gly Gly Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Met Gly Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 166
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 166
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Val Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Trp Asp Glu Asp
65 70 75 80
Leu Leu Asp Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Met Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Val Gly Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys

145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 167
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 167
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Ile Pro Arg Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Glu Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Asp
65 70 75 80
Leu Leu Asp Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Met Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 168
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
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<400> 168
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20 25 30
Arg Tyr Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Val Ala Trp Asp Glu Arg
65 70 75 80
Leu Leu Asp Lys Leu Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Ile Ala Leu Met
100 105 110

Asn Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 169
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 169
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Glu Gly Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Leu Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 170
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
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<400> 170
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Leu Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Glu Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser

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65                  70                      75                      80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                  90                      95
Glu Ala Cys Val Ile Gln Glu Val Gly Met Glu Glu Thr Pro Leu Met
            100                 105                     110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                     125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                     140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                     155                 160
Arg Leu Arg Arg Lys Glu
                165
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<210> 171
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 171

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Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
 1               5                  10                      15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                      30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                      45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                      60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Asp Glu Thr
65                  70                      75                      80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                  90                      95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Thr Glu Thr Pro Leu Met
            100                 105                     110
Lys Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                     125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                     140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                     155                 160
Arg Leu Arg Arg Lys Glu
                165
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<210> 172
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 172

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Cys Asp Leu Pro Gln Thr His Ser Leu Asn Asn Arg Arg Thr Leu Met
 1               5                  10                      15
Leu Met Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                      30
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Arg His Asp Phe Glu Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Leu Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Asp Thr Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 173
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 173
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1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Met Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Tyr Gln Gln Leu Asn Asn Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 174
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 174
Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Met Met
1 5 10 15
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20 25 30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly His Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Val Met Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Met Glu Glu Thr Pro Leu Met
100 105 110
Asn Val Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 175
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 175
Cys Asp Leu Pro Gln Thr His Ser Leu Asp Asn Arg Arg Thr Leu Met
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Ala Phe His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Asp Thr Trp Asp Ala Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Val Asp Ser Ile Leu Thr Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 176
<211> 166
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 176

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Cys Asp Leu Pro Gln Thr His Ser Leu Asp Asn Arg Arg Thr Leu Met
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Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Arg Ile Pro Gln Glu Val Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Glu Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Asp Lys Phe Tyr Ile Glu Leu Phe Gln Gln Met Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Thr Gln Glu Val Gly Val Glu Glu Ile Ala Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
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<210> 177
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 177

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Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Met Met
1               5                   10                  15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Asp Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Met Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Asp Thr Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Phe Gln Gln Met Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
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<210> 178
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 178
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Arg
100 105 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 179
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 179
Cys Asp Leu Pro Gln Thr His Ser Leu Asp Asn Arg Arg Thr Leu Met
1 5 10 15
Leu Met Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Phe Pro Gln Glu Val Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Ala Phe His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Met Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ser Trp Glu Val Val

130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 180
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 180
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Ser Arg Arg Thr Leu Met
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Leu Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu Tyr Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Thr Trp Glu Gln Ser
65 70 75 80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Gly Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 181
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 181
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Ile Pro Arg Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Glu Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Trp Asp Glu Asp
65 70 75 80
Leu Leu Asp Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95

Glu Ala Cys Met Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Ile Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 182
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 182
Cys Asp Leu Pro Gln Thr His Ser Leu Asn Asn Arg Arg Thr Leu Met
1 5 10 15
Leu Met Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Asp Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Met Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 183
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 183
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg Tyr Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly His Gln Phe
35 40 45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Leu Met Gln Gln Thr

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    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Glu Gln Ser
65                  70                  75                  80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
            100                 105                 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165


<210> 184
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 184
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
 1               5                  10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Leu Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Val Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65                  70                  75                  80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
            100                 105                 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165


<210> 185
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 185
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
 1               5                  10                  15
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Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Leu Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Asp Thr Trp Asp Ala Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Val Asp Ser Ile Leu Thr Val Arg Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 186
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 186
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Glu Gly Glu Phe Asp Gly His Gln Phe
35 40 45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Met Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Thr Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Phe Gln Gln Met Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 187
<211> 166
<212> PRT
<213> Artificial Sequence

<220>

<223> Synthetic IFN-alpha Polypeptide

<400> 187

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Cys Asp Leu Pro Gln Thr His Ser Leu Ser Asn Arg Arg Thr Leu Met
1               5                   10                  15
Ile Met Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Leu Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65                  70                  75                  80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Gly Glu Thr Pro Leu Met
            100                 105                 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
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<210> 188
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 188

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Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65                  70                  75                  80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Asn Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
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<210> 189

<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 189
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Leu Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Met Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Asp Thr Trp Asp Ala Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met
100 105 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 190
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 190
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Gly Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Ile Pro Gln Glu Val Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Ile Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Ile
100 105 110
Asn Val Asp Pro Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160

Arg Leu Arg Arg Lys Glu
165

<210> 191
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 191
Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Met Met
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Thr Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Leu Phe Gln Gln Thr
50 55 60
Phe Asn Leu Phe Thr Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 192
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 192
Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Met Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Ile Glu Leu Asn Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
100 105 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr

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        115                     120                 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                     135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
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<210> 193
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 193

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Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1               5                   10                  15
Leu Leu Gly Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Phe Gln Gln Met Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
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<210> 194
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 194

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Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Leu Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Thr Trp Asp Glu Thr
65                  70                  75                  80
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Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 195
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 195
Cys Asp Leu Pro Gln Thr His Ser Leu Ser Asn Arg Arg Thr Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Glu Phe Pro Gln Glu Glu Phe Asp Asp Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Val Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 196
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 196
Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Met Met
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly His Gln Phe

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        35                  40                      45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Leu Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65                  70                  75                  80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Phe Gln Gln Met Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met
            100                 105                 110
Lys Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
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<210> 197
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 197

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Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Met Met
1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Arg Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Met Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys His Ser Ser Ala Thr Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Asp Lys Phe Tyr Ile Glu Leu Asn Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
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<210> 198
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 198

Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Met Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Phe Gln Gln Met Asn Asp Leu
85 90 95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
100 105 110
Asn Ala Ala Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 199
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 199
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Val Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
100 105 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 200
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 200
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Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1               5                   10                  15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Arg Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Glu Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Trp Asp Glu Asp
65                  70                  75                  80
Leu Leu Asp Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Met Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Val Gly Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
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<210> 201
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 201
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Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Leu Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65                  70                  75                  80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
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<210> 202
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 202
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Ala Phe His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
100 105 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ser Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 203
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 203
Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Met Met
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Leu Pro Gln Glu Glu Phe Asp Gly His Gln Phe
35 40 45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Met Arg Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Asp Thr Trp Asp Ala Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Ile Ala Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140

Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 204
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 204
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Leu Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Glu Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Asp Lys Phe Arg Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
100 105 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ser Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 205
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 205
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Phe Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Trp Asp Glu Asp
65 70 75 80
Leu Leu Asp Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Met Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met

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                100                     105                     110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                     120                     125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                     135                     140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                     150                     155                     160
Arg Leu Arg Arg Lys Glu
                165
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<210> 206
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 206

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Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Glu Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Thr Trp Glu Gln Ser
65                  70                  75                  80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 207
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 207

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Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1               5                   10                  15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Leu Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
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Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Pro Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 208
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 208
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Met
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Glu Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Glu Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Asp Glu Asp
65 70 75 80
Leu Leu Asp Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Arg
100 105 110
Asn Val Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 209
<211> 164
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 209
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp

```
            20                      25                      30
Arg His Asp Phe Arg Ile Pro Arg Glu Glu Phe Asp Gly Asn Gln Phe
        35                      40                      45
Gln Lys Ala Glu Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
    50                      55                      60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65                      70                      75                      80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                      90                      95
Glu Ala Cys Val Ile Gln Gly Val Gly Glu Thr Pro Leu Met Asn Glu
            100                     105                     110
Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu Tyr
        115                     120                     125
Leu Val Gly Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg Ala
    130                     135                     140
Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys Arg Leu
145                     150                     155                     160
Arg Arg Lys Glu
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<210> 210
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 210

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Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Met Met
1               5                   10                  15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Ala Phe His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Phe Gln Gln Met Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met
            100                 105                 110
Asn Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 211
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 211
Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Glu Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Thr Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 212
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 212
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Ile Pro Gln Glu Val Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Glu Thr Ile Pro Val Leu His Glu Val Ile Gln Arg Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 213
<211> 166

<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 213
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Met Glu Glu Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 214
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 214
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Met Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Phe Arg Gln Met Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Arg
100 105 110
Asn Val Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu

165

<210> 215
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 215
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1   5   10   15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20   25   30
Arg His Asp Phe Arg Ile Pro Arg Glu Glu Phe Asp Gly Asn Gln Phe
        35   40   45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50   55   60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Thr Trp Glu Gln Ser
65   70   75   80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85   90   95
Glu Ser Cys Val Met Gln Glu Val Gly Val Glu Glu Thr Pro Leu Ile
            100   105   110
Asn Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
        115   120   125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130   135   140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145   150   155   160
Arg Leu Arg Arg Lys Glu
                165

<210> 216
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 216
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1   5   10   15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20   25   30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly His Gln Phe
        35   40   45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50   55   60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Arg
65   70   75   80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85   90   95
Glu Ser Cys Val Met Gln Glu Val Gly Val Thr Gly Thr Pro Leu Met
            100   105   110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115   120   125

Leu Tyr Leu Met Glu Lys Lys Tyr Gly Pro Cys Ala Trp Glu Val Val
    130   135   140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145   150   155   160
Arg Leu Arg Arg Lys Glu
                165

<210> 217
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 217
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1   5   10   15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20   25   30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35   40   45
Gln Lys Ala Pro Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
    50   55   60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65   70   75   80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85   90   95
Glu Ser Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
            100   105   110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115   120   125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130   135   140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145   150   155   160
Arg Leu Arg Arg Lys Glu
                165

<210> 218
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 218
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1   5   10   15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20   25   30
Arg His Asp Phe Gly Leu Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35   40   45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Met Gln Gln Thr
    50   55   60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65   70   75   80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu

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                        85                        90                        95
Glu Ala Cys Val Met Gln Glu Val Gly Met Glu Glu Thr Pro Leu Met
            100                     105                     110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                     120                     125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                     135                     140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                     150                     155                     160
Arg Leu Arg Arg Lys Glu
                165
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<210> 219
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 219

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Cys Asp Leu Pro Gln Thr His Ser Leu Asn Asn Arg Arg Thr Leu Met
1               5                   10                  15
Leu Met Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly His Gln Phe
        35                  40                  45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ser Cys Val Met Gln Glu Val Gly Val Ile Glu Ser Pro Leu Met
            100                 105                 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 220
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 220

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Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1               5                   10                  15
Leu Leu Ala Gln Met Arg Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
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Gln Lys Ala Pro Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ser Cys Val Met Gln Glu Val Gly Val Ile Glu Ser Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Ala
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Ala Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 221
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 221
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Leu Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ser Cys Val Met Gln Glu Val Gly Val Ile Glu Ser Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 222
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 222
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile

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 1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly His Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Glu Lys Phe Cys Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
            100                 105                 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Ile
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
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<210> 223
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 223

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Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
 1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Arg Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Val Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65                  70                  75                  80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
            100                 105                 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ser Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
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<210> 224
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 224
Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Leu Met
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly His Gln Phe
35 40 45
Gln Lys Ala Pro Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ser Cys Val Met Gln Glu Val Gly Val Ile Glu Ser Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 225
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 225
Cys Asp Leu Pro Gln Thr His Ser Leu Asn Asn Arg Arg Thr Leu Met
1 5 10 15
Leu Met Ala Gln Met Arg Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg Tyr Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Phe Arg Gln Met Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Arg
100 105 110
Asn Val Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 226
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 226
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu Leu Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Ile Glu Leu Phe Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Arg
100 105 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 227
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 227
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Pro Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Asp
65 70 75 80
Leu Leu Asp Lys Phe Cys Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys

145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 228
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 228
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Thr Gln Met Arg Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Glu Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Val Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 229
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 229
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Gly Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Ile Pro Gln Glu Val Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Thr Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ser Cys Val Met Gln Glu Val Gly Val Glu Glu Thr Pro Leu Ile
100 105 110

Asn Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
        115   120   125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130   135   140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145   150   155   160
Arg Leu Arg Arg Lys Glu
                165

<210> 230
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 230
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1   5   10   15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20   25   30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35   40   45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50   55   60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Trp Asp Glu Asp
65   70   75   80
Leu Leu Asp Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85   90   95
Glu Ala Cys Met Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100   105   110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115   120   125
Leu Tyr Leu Val Gly Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130   135   140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145   150   155   160
Arg Leu Arg Arg Lys Glu
                165

<210> 231
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 231
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1   5   10   15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20   25   30
Arg His Asp Phe Arg Ile Pro Arg Glu Glu Phe Asp Gly Asn Gln Phe
        35   40   45
Gln Lys Ala Glu Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
    50   55   60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr

65 70 75 80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ser Cys Val Met Gln Glu Val Gly Val Ile Glu Ser Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 232
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 232
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Ile Pro Arg Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Glu Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ser Cys Val Met Gln Glu Val Gly Val Thr Gly Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 233
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 233
Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Met Met
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30

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Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly His Gln Phe
        35                  40                  45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65                  70                  75                  80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Met Gln Glu Val Trp Val Gly Gly Thr Pro Leu Met
            100                 105                 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
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<210> 234
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 234

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Cys Asp Leu Pro Gln Thr His Ser Leu Ser Asn Arg Arg Thr Leu Ile
1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Glu Phe Pro Gln Glu Glu Phe Asp Asp Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Glu Gln Ser
65                  70                  75                  80
Leu Leu Asp Lys Phe Tyr Ile Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
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<210> 235
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 235
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Leu Pro Gln Glu Glu Phe Asp Gly Asp Gln Phe
35 40 45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Asp Thr Trp Asp Ala Thr
65 70 75 80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Leu Gly Val Gly Val Thr Glu Thr Pro Leu Met
100 105 110
Lys Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 236
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 236
Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Met Met
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Leu Pro Gln Glu Val Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Ala Phe His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Thr Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ser Cys Val Met Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Met Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 237
<211> 166
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 237
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1   5   10   15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20   25   30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly His Gln Phe
        35   40   45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50   55   60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65   70   75   80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
                85   90   95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100   105   110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115   120   125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130   135   140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145   150   155   160
Arg Leu Arg Arg Lys Glu
                165

<210> 238
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 238
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1   5   10   15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20   25   30
Arg His Asp Phe Arg Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35   40   45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50   55   60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Trp Asp Glu Thr
65   70   75   80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85   90   95
Glu Ser Cys Val Met Gln Glu Val Gly Val Ile Glu Ser Pro Leu Met
            100   105   110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115   120   125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130   135   140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145   150   155   160
Arg Leu Arg Arg Lys Glu
                165

<210> 239
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 239
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly His Gln Phe
35 40 45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Arg
65 70 75 80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ser Cys Val Met Gln Glu Val Gly Val Thr Gly Thr Pro Leu Arg
100 105 110
Asn Val Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 240
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 240
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Pro Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ser Cys Val Met Gln Glu Val Gly Val Ile Glu Ser Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val

130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 241
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 241
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly His Gln Phe
35 40 45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Arg
65 70 75 80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ser Cys Val Met Gln Glu Val Gly Val Thr Gly Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 242
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 242
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Pro Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Thr Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95

Glu Ala Cys Val Met Gln Gly Glu Arg Val Gly Glu Thr Pro Leu Arg
100 105 110
Asn Val Asp Ser Ile Leu Thr Val Arg Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 243
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 243
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Val
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly His Gln Phe
35 40 45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Asn Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Arg
65 70 75 80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ser Cys Val Met Gln Glu Val Gly Val Thr Gly Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 244
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 244
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Val Gln Gln Thr

```
    50                  55                  60
Phe Asn Leu Phe Asn Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65                  70                  75                  80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
            100                 105                 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ser Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Thr Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165


<210> 245
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 245
Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Met Met
 1              5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Thr Trp Glu Gln Ser
65                  70                  75                  80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ser Cys Val Met Gln Glu Val Gly Val Glu Glu Thr Pro Leu Ile
            100                 105                 110
Asn Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165


<210> 246
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 246
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
 1              5                   10                  15
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Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg Tyr Asp Phe Glu Phe Pro Gln Glu Glu Phe Asp Gly His Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Met Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Leu Asp Glu Thr
65 70 75 80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ser Cys Val Met Gln Glu Val Gly Val Thr Gly Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 247
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 247
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met
100 105 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 248
<211> 166
<212> PRT
<213> Artificial Sequence

<220>

<223> Synthetic IFN-alpha Polypeptide

<400> 248
```
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Thr Met Met
 1               5                  10                  15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Phe Gln Gln Met Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Arg
            100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Lys Lys Lys Tyr Ser Pro Cys Ser Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 249
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 249
```
Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Met Met
 1               5                  10                  15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly His Gln Phe
        35                  40                  45
Gln Lys Thr Gln Ala Ile Ser Val His His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65                  70                  75                  80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 250

<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 250
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly His Gln Phe
35 40 45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Arg
65 70 75 80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ser Cys Val Met Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 251
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 251
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Leu Asp Glu Thr
65 70 75 80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Asn Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Ala Leu Met
100 105 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Glu Lys
145 150 155 160

Arg Leu Arg Arg Lys Glu
165

<210> 252
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 252
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Glu Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Thr Trp Asp Ala Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Gly Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 253
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 253
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Leu Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Phe Arg Gln Met Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Arg
100 105 110
Asn Val Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr

```
        115                 120                 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 254
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 254

```
Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Met Met
 1               5                  10                  15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Arg Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65                  70                  75                  80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 255
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 255

```
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
 1               5                  10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly His Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Leu Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65                  70                  75                  80
```

```
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 256
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 256

```
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
 1              5                   10                  15
Leu Leu Ala Gln Met Arg Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Glu Phe Arg Phe Pro Glu Glu Glu Phe Asp Ser Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Asp Thr Trp Asp Ala Thr
65                  70                  75                  80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Leu Gly Val Gly Val Thr Glu Thr Pro Leu Met
            100                 105                 110
Lys Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 257
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 257

```
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
 1              5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Glu Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
```

```
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65                  70                  75                  80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Met Gln Lys Val Gly Val Glu Glu Thr Pro Leu Arg
            100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Ser Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165


<210> 258
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 258
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Glu Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Asp Thr Trp Asp Ala Thr
65                  70                  75                  80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ser Cys Val Ile Gln Glu Val Gly Val Glu Glu Ile Ala Leu Met
            100                 105                 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165


<210> 259
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 259
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```
Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Met Met
 1               5                  10                  15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Arg Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Thr Trp Glu Gln Ser
65                  70                  75                  80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Thr Val Arg Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ser Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 260
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 260

```
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
 1               5                  10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Leu Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65                  70                  75                  80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Val Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 261
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 261
Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Met Met
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Met Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys His Ser Ser Ala Thr Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Ile Glu Leu Asn Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Val Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 262
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 262
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Leu Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Arg
65 70 75 80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ser Cys Val Met Gln Glu Val Gly Val Thr Gly Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 263
<211> 165
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 263
Cys Asp Leu Pro Gln Thr His Ser Leu Asp Asn Arg Arg Thr Leu Met
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Lys Gln Phe Gln
35 40 45
Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr Phe
50 55 60
Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Trp Asp Glu Asp Leu
65 70 75 80
Leu Asp Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu Glu
85 90 95
Ser Cys Val Met Gln Glu Val Gly Val Ile Glu Ser Pro Leu Met Asn
100 105 110
Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr Leu
115 120 125
Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
130 135 140
Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys Arg
145 150 155 160
Leu Arg Arg Lys Glu
165

<210> 264
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 264
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly His Gln Phe
35 40 45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Arg
65 70 75 80
Leu Leu Glu Lys Phe Tyr Thr Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ser Cys Val Met Gln Glu Val Gly Val Thr Gly Ala Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140

Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 265
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 265
Cys Asp Leu Pro Gln Thr His Ser Leu Ser Asn Arg Arg Thr Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Asn Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Arg
100 105 110
Asn Val Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ser Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 266
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 266
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Thr Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ser Cys Val Met Gln Glu Val Gly Val Glu Glu Thr Pro Leu Ile

100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 267
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 267
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Met
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Leu Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Thr Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 268
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 268
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Thr Met Met
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Phe Pro Gln Glu Val Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60

Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Thr Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 269
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 269
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Met Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Asp Thr Trp Asp Val Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Gly Glu Thr Pro Leu Met
100 105 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 270
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 270
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp

```
                20                  25                  30
Arg His Asp Phe Gly Leu Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Thr Trp Glu Gln Ser
65                  70                  75                  80
Leu Leu Glu Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Gly Glu Thr Pro Leu Met
            100                 105                 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 271
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 271

```
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
 1               5                  10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Arg Ile Pro Arg Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Glu Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Leu Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 272
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 272

Cys Asp Leu Pro Gln Thr His Ser Leu Ser Asn Arg Arg Thr Leu Ile
1   5   10   15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20   25   30
Arg His Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35   40   45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Met Gln Gln Thr
    50   55   60
Phe Asn Leu Phe Ser Thr Lys His Ser Ser Ala Thr Trp Asp Glu Thr
65   70   75   80
Leu Leu Asp Lys Phe Tyr Ile Glu Leu Asn Gln Gln Leu Asn Asp Leu
                85   90   95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100   105   110
Asn Val Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
        115   120   125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130   135   140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145   150   155   160
Arg Leu Arg Arg Lys Glu
                165

<210> 273
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 273

Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1   5   10   15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20   25   30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly His Gln Phe
        35   40   45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Val Met Gln Gln Thr
    50   55   60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Trp Glu Gln Ser
65   70   75   80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85   90   95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Gly Glu Thr Pro Leu Met
            100   105   110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115   120   125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130   135   140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145   150   155   160
Arg Leu Arg Arg Lys Glu
                165

<210> 274
<211> 166

<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 274
```
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
 1               5                  10                  15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Thr Trp Glu Gln Ser
65                  70                  75                  80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ser Cys Val Met Gln Glu Val Gly Val Glu Glu Thr Pro Leu Ile
            100                 105                 110
Asn Val Asp Pro Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Lys Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 275
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 275
```
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
 1               5                  10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Glu Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Thr Gln Ala Ile Ser Ala Phe His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Asp Thr Trp Asp Ala Thr
65                  70                  75                  80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Thr Gln Glu Val Gly Met Glu Glu Thr Pro Leu Arg
            100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
```

165

<210> 276
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 276
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Gly Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Ile Pro Gln Glu Val Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Ile Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 277
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 277
Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Met Met
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Ile Pro Gln Glu Val Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ser Cys Val Met Gln Glu Val Gly Val Glu Glu Thr Pro Leu Ile
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
115 120 125

Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130   135   140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145   150   155   160
Arg Leu Arg Arg Lys Glu
                165

<210> 278
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 278
Cys Asp Leu Pro Gln Thr His Ser Leu Ser Asn Arg Arg Thr Leu Ile
1   5   10   15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20   25   30
Arg His Asp Phe Glu Phe Pro Gln Glu Glu Phe Asp Asp Asn Gln Phe
        35   40   45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50   55   60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65   70   75   80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
                85   90   95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100   105   110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115   120   125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130   135   140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145   150   155   160
Arg Leu Arg Arg Lys Glu
                165

<210> 279
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 279
Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Met Met
1   5   10   15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20   25   30
Arg His Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35   40   45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
    50   55   60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Thr Trp Glu Gln Ser
65   70   75   80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu

```
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Thr Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 280
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 280

```
Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Leu Met
1               5                   10                  15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly His Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Val Met Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys His Ser Ser Ala Thr Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Asp Lys Phe Tyr Ile Glu Leu Asn Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 281
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 281

```
Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Met Met
1               5                   10                  15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Arg Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
```

Gln Lys Ala Glu Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
50 55 60
Ser Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Phe Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
100 105 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 282
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 282
Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Met Met
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly His Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Val Met Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Gly Glu Thr Pro Leu Met
100 105 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 283
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 283
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Phe Ile

```
1                   5                       10                      15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
                20                  25                  30
Arg His Asp Phe Arg Ile Pro Gln Glu Val Phe Asp Gly Asn Gln Phe
            35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
        50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Glu Gln Ser
65                  70                  75                      80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Met Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                     160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 284
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 284

```
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1               5                   10                  15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Leu Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Glu Gln Ser
65                  70                  75                  80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
            100                 105                 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 285
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 285
```
Cys Asp Leu Pro Gln Thr His Ser Leu Asn Asn Arg Arg Thr Leu Met
 1               5                  10                  15
Leu Met Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Glu Phe Pro Gln Glu Glu Phe Asp Asp Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Glu Gln Ser
65                  70                  75                  80
Leu Leu Asp Lys Phe Tyr Ile Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Gly Glu Thr Pro Leu Met
            100                 105                 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 286
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 286
```
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
 1               5                  10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Ser Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Pro Ala Ile Ser Ala Phe His Glu Met Ile His Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Met Gln Glu Val Gly Val Glu Asp Thr Pro Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 287
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 287
Cys Asp Leu Pro Gln Thr His Ser Leu Ser His Arg Arg Thr Leu Met
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Arg Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Asp Ala Trp Asp Ala Thr
65 70 75 80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Ala Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 288
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 288
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Glu Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
100 105 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys

145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 289
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 289
Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Met Met
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
100 105 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 290
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 290
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Leu Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
100 105 110

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Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
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<210> 291
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 291
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Arg Phe Pro Gln Glu Glu Phe Asp Gly His Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65                  70                  75                  80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Phe Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Thr Val Arg Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ser Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
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<210> 292
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 292
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys His Ser Ser Ala Thr Trp Asp Glu Thr
```

```
65                  70                  75                  80
Leu Leu Asp Lys Phe Tyr Ile Glu Leu Asn Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 293
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 293

```
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Leu Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Leu Asp Glu Thr
65                  70                  75                  80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Met Gln Glu Val Trp Val Gly Gly Thr Pro Leu Met
            100                 105                 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 294
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 294

```
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
```

```
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Pro Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ser Cys Val Met Gln Glu Val Gly Val Ile Glu Ser Pro Leu Met
            100                 105                 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 295
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 295

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Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1               5                   10                  15
Leu Leu Gly Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65                  70                  75                  80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
            100                 105                 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 296
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 296
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
100 105 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 297
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 297
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly His Gln Phe
35 40 45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Arg
65 70 75 80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ser Cys Val Met Gln Glu Val Gly Val Thr Gly Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 298
<211> 166
<212> PRT

<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 298
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Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Glu Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 299
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 299
```
Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Met Met
1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Met Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys His Ser Ser Ala Thr Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Asp Lys Phe Tyr Ile Glu Leu Asn Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 300
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 300
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Thr Gln Glu Val Gly Val Glu Glu Ile Ala Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 301
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 301
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Glu Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Pro Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Phe Gln Gln Met Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Arg
100 105 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val

130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 302
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 302
Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Met Met
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Leu Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Arg Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Ala Asp Ser Ile Leu Pro Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 303
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 303
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Glu Phe Arg Phe Pro Glu Glu Glu Phe Asp Ser Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Asp Thr Trp Asp Ala Thr
65 70 75 80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95

```
Glu Ala Cys Val Ile Leu Gly Val Gly Val Thr Glu Thr Pro Leu Met
            100                 105                 110
Lys Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 304
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 304

```
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
 1               5                  10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly His Gln Phe
        35                  40                  45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Arg
65                  70                  75                  80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ser Cys Val Met Gln Glu Val Gly Val Thr Gly Thr Pro Leu Met
            100                 105                 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Gly Leu Arg Arg Lys Glu
                165
```

<210> 305
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 305

```
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
 1               5                  10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Pro Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
```

```
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ser Cys Val Met Gln Glu Val Gly Val Ile Glu Ser Pro Leu Met
            100                 105                 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165


<210> 306
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 306
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Phe Ile
1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Trp Asp Glu Asp
65                  70                  75                  80
Leu Leu Asp Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Met Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Val Gly Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165


<210> 307
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 307
Cys Asp Leu Pro Gln Thr His Ser Leu Asp Asn Arg Arg Thr Leu Met
1               5                   10                  15
```

```
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Ala Phe His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65                  70                  75                  80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Gly Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 308
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 308

```
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Trp Asp Glu Asp
65                  70                  75                  80
Leu Leu Asp Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Met Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Val Gly Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 309
<211> 166
<212> PRT
<213> Artificial Sequence

<220>

<223> Synthetic IFN-alpha Polypeptide

<400> 309
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Val Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
100 105 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ser Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 310
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 310
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly His Gln Phe
35 40 45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Arg
65 70 75 80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ser Cys Val Met Gln Glu Val Gly Val Thr Gly Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 311

<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 311
```
Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Met Met
 1               5                   10                  15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly His Gln Phe
        35                  40                  45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65                  70                  75                  80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Met Gln Glu Val Trp Val Gly Gly Thr Pro Leu Met
            100                 105                 110
Asn Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 312
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 312
```
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
 1               5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly His Gln Phe
        35                  40                  45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Arg
65                  70                  75                  80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ser Cys Val Met Gln Glu Val Gly Val Thr Gly Thr Pro Leu Met
            100                 105                 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
```

Arg Leu Arg Arg Lys Glu
165

<210> 313
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 313
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser His Phe Ser Cys Leu Lys Asp
20 25 30
Arg Tyr Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly His Gln Phe
35 40 45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Asp Glu Thr
65 70 75 80
Leu Leu Asp Glu Phe Tyr Val Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Ile Ala Leu Met
100 105 110
Asn Glu Asp Phe Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 314
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 314
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Pro Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
100 105 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr

115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 315
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 315
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Ile Pro Arg Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Glu Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Trp Asp Glu Asp
65 70 75 80
Leu Leu Asp Lys Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Met Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Glu Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Lys Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 316
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 316
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Thr Met Met
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Thr Trp Glu Gln Ser
65 70 75 80

Leu Leu Glu Lys Phe Ser Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 317
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 317
Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Leu Met
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly His Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Val Met Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Gly Glu Thr Pro Leu Met
100 105 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Glu
165

<210> 318
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 318
Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Leu Met
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly His Gln Phe

```
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Val Met Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Trp Glu Gln Ser
65                  70                  75                  80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Gly Glu Thr Pro Leu Met
            100                 105                 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 319
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic IFN-alpha Polypeptide

<400> 319

```
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
 1               5                  10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Arg Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Met Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys His Ser Ser Ala Thr Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Asp Lys Phe Tyr Ile Glu Leu Asn Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165
```

<210> 320
<211> 166
<212> PRT
<213> Homo Sapiens

<400> 320

```
Cys Asp Leu Pro Glu Thr His Ser Leu Asp Asn Arg Arg Thr Leu Met
 1               5                  10                  15
Leu Leu Ala Gln Met Ser Arg Ile Ser Pro Ser Ser Cys Leu Met Asp
```

```
                20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
            35                  40                  45
Gln Lys Ala Pro Ala Ile Ser Val Leu His Glu Leu Ile Gln Gln Ile
        50                  55                  60
Phe Asn Leu Phe Thr Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Asp
65                  70                  75                  80
Leu Leu Asp Lys Phe Cys Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Met Gln Glu Glu Arg Val Gly Glu Thr Pro Leu Met
            100                 105                 110
Asn Ala Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Arg Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Leu Ser Leu Ser Thr Asn Leu Gln Glu
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165


<210> 321
<211> 165
<212> PRT
<213> Homo Sapiens

<400> 321
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met
 1               5                  10                  15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
        35                  40                  45
Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
    50                  55                  60
Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
65                  70                  75                  80
Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
                85                  90                  95
Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
            100                 105                 110
Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
        115                 120                 125
Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
    130                 135                 140
Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser
145                 150                 155                 160
Leu Arg Ser Lys Glu
                165


<210> 322
<211> 165
<212> PRT
<213> Homo Sapiens

<400> 322
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met
 1               5                  10                  15
Leu Leu Ala Gln Met Arg Lys Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
```

Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
35 40 45
Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
50 55 60
Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
65 70 75 80
Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
85 90 95
Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
100 105 110
Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
115 120 125
Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
130 135 140
Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser
145 150 155 160
Leu Arg Ser Lys Glu
165

<210> 323
<211> 166
<212> PRT
<213> Homo Sapiens

<400> 323
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Gly Arg Ile Ser His Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Glu Glu Glu Phe Asp Gly His Gln Phe
35 40 45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Val Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Leu Ser Phe Ser Thr Asn Leu Gln Lys
145 150 155 160
Arg Leu Arg Arg Lys Asp
165

<210> 324
<211> 166
<212> PRT
<213> Homo Sapiens

<400> 324
Cys Asp Leu Pro Gln Thr His Ser Leu Ser Asn Arg Arg Thr Leu Met
1 5 10 15
Ile Met Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe

```
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Thr Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Met Met Gln Glu Val Gly Val Glu Asp Thr Pro Leu Met
            100                 105                 110
Asn Val Asp Ser Ile Leu Thr Val Arg Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Ala Asn Leu Gln Glu
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165


<210> 325
<211> 166
<212> PRT
<213> Homo Sapiens

<400> 325
Cys Asp Leu Pro Gln Thr His Ser Leu Gly His Arg Arg Thr Met Met
 1               5                  10                  15
Leu Leu Ala Gln Met Arg Arg Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Arg Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Glu Ala Ile Ser Val Leu His Glu Val Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Val Ala Trp Asp Glu Arg
65                  70                  75                  80
Leu Leu Asp Lys Leu Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Met Gln Glu Val Trp Val Gly Gly Thr Pro Leu Met
            100                 105                 110
Asn Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Ser Ser Arg Asn Leu Gln Glu
145                 150                 155                 160
Arg Leu Arg Arg Lys Glu
                165


<210> 326
<211> 166
<212> PRT
<213> Homo Sapiens

<400> 326
Cys Asp Leu Pro Gln Thr His Ser Leu Arg Asn Arg Arg Ala Leu Ile
 1               5                  10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Glu Phe Arg Phe Pro Glu Glu Glu Phe Asp Gly His Gln Phe
        35                  40                  45
```

Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Glu Asp Phe Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Lys Lys
145 150 155 160
Gly Leu Arg Arg Lys Asp
165

<210> 327
<211> 166
<212> PRT
<213> Homo Sapiens

<400> 327
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Ala Gln Met Arg Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Glu Phe Pro Gln Glu Glu Phe Asp Asp Lys Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
50 55 60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Leu Asp Glu Thr
65 70 75 80
Leu Leu Asp Glu Phe Tyr Ile Glu Leu Asp Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ser Cys Val Met Gln Glu Val Gly Val Ile Glu Ser Pro Leu Met
100 105 110
Tyr Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Ser Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Ile Asn Leu Gln Lys
145 150 155 160
Arg Leu Lys Ser Lys Glu
165

<210> 328
<211> 166
<212> PRT
<213> Homo Sapiens

<400> 328
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
1 5 10 15
Leu Leu Gly Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
20 25 30
Arg His Asp Phe Arg Ile Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
35 40 45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr

```
    50                  55                  60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65                  70                  75                  80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Ile Glu Arg Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Leu Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Asp
                165
```

<210> 329
<211> 166
<212> PRT
<213> Homo Sapiens

<400> 329

```
Cys Asn Leu Ser Gln Thr His Ser Leu Asn Asn Arg Arg Thr Leu Met
 1              5                   10                  15
Leu Met Ala Gln Met Arg Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Glu Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Met Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asn Ser Ser Ala Ala Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Glu Lys Phe Tyr Ile Glu Leu Phe Gln Gln Met Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Met Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Arg Leu Arg Arg Lys Asp
                165
```

<210> 330
<211> 166
<212> PRT
<213> Homo Sapiens

<400> 330

```
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
 1              5                   10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser His Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg Tyr Asp Phe Gly Phe Pro Gln Glu Val Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Ala Phe His Glu Met Ile Gln Gln Thr
    50                  55                  60
```

```
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr
65                  70                  75                  80
Leu Leu Asp Lys Phe Tyr Ile Glu Leu Phe Gln Gln Leu Asn Asp Leu
                85                  90                  95
Glu Ala Cys Val Thr Gln Glu Val Gly Val Glu Glu Ile Ala Leu Met
            100                 105                 110
Asn Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Met Gly Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Phe Ser Thr Asn Leu Gln Lys
145                 150                 155                 160
Gly Leu Arg Arg Lys Asp
                165
```

<210> 331
<211> 166
<212> PRT
<213> Homo Sapiens

<400> 331

```
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Asn Arg Arg Ala Leu Ile
 1               5                  10                  15
Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Leu Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Thr Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Glu Asp Ser Ser Ala Ala Trp Glu Gln Ser
65                  70                  75                  80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Tyr Gln Gln Leu Asn Asn Leu
                85                  90                  95
Glu Ala Cys Val Ile Gln Glu Val Gly Met Glu Glu Thr Pro Leu Met
            100                 105                 110
Asn Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr
        115                 120                 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
    130                 135                 140
Arg Ala Glu Ile Met Arg Ser Leu Ser Phe Ser Thr Asn Leu Gln Lys
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Ile Leu Arg Arg Lys Asp
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<213> Homo Sapiens

<400> 332

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Leu Leu Ala Gln Met Gly Arg Ile Ser Pro Phe Ser Cys Leu Lys Asp
            20                  25                  30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln Phe
        35                  40                  45
Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln Thr
    50                  55                  60
Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Thr Trp Glu Gln Ser
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65 70 75 80
Leu Leu Glu Lys Phe Ser Thr Glu Leu Asn Gln Gln Leu Asn Asp Leu
85 90 95
Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu Met
100 105 110
Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile Thr
115 120 125
Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val
130 135 140
Arg Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Lys Ile Phe Gln Glu
145 150 155 160
Arg Leu Arg Arg Lys Glu
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Ile Leu Leu Ala Gln Met Arg Arg Ile Ser Pro Phe Ser Cys Leu Lys
20 25 30
Asp Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Asp Gly Asn Gln
35 40 45
Phe Gln Lys Ala Gln Ala Ile Ser Val Leu His Glu Met Ile Gln Gln
50 55 60
Thr Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu
65 70 75 80
Ser Leu Leu Glu Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp
85 90 95
Leu Glu Ala Cys Val Ile Gln Glu Val Gly Val Glu Glu Thr Pro Leu
100 105 110
Met Asn Val Asp Ser Ile Leu Ala Val Lys Lys Tyr Phe Gln Arg Ile
115 120 125
Thr Leu Tyr Leu Thr Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val
130 135 140
Val Arg Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln
145 150 155 160
Glu Arg Leu Arg Arg Lys Glu
165

<210> 334
<211> 13
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Gly Ala Pro Val Pro Tyr Pro Asp Pro Leu Glu Pro Arg
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<210> 335
<211> 15
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<220>
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<400> 335
Lys Glu Thr Ala Ala Ala Lys Phe Glu Arg Gln His Met Asp Ser
1 5 10 15